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PREGNANCY OUTCOMES IN SANTA CLARA COUNTY 1980-1982

REPORTS OF TWO EPIDEMIOLOGICAL STUDIES

GEORGE DEUKMEJIAN
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FORWORD

This report presents the results of two related studies of pregnancy outcomes conducted by the Epidemiological Studies Section of the California Department of Health Services (CDHS), with the cooperation of the Santa Clara County Department of Health. The studies were carried out in response to citizens who reported birth defects and miscarriages in the Los Paseos neighborhood of San Jose. The citizens made their concerns public after learning that their drinking water had been contaminated by a chemical leak from an underground tank at a nearby company.

The first study in this report is an investigation of congenital heart defects occurring in infants born in Santa Clara County in 1981 and 1982. This study is based on a review of medical records in all hospitals likely to treat children from Santa Clara County.

The second study focused on the Los Paseos census tract. Women who had been pregnant in 1980 and 1981 were interviewed and compared to women who had been pregnant in a census tract 4 miles to the north. Measurements of water quality taken there showed no evidence of chemical contamination in 1982. This study investigated miscarriages, birth weight and birth defects of all kinds.

The design of the two studies were developed in consultation with a committee of health professionals and community representatives (see acknowledgements).

During the last phase of the investigation a technical committee of outside university and government experts reviewed each phase of the analysis. One member of this committee was named by a local citizens group and another by local industry. All committee members agreed to keep the results confidential until the formal release of the final report (see acknowledgements).

These studies are unusual in the extent to which efforts were made to assess and control sources of potential bias. For example, almost all the abnormalities reported in the studies were medically verified. The records of a sample of women who had moved from the area before the interview were reviewed to make sure that those who had moved away were no different from those who had stayed. The records of a sample of women who had not recalled being pregnant were reviewed to determine whether under-reporting of miscarriages was biasing the study results. These efforts required that nineteen individuals in the Epidemiological Studies Section devoted more than 10,000 person hours (about 5 person years) to this study. The results which are reported here, therefore, represent an unusually intense and careful effort to investigate a health problem which community members believed to be related to an environmental exposure.

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The Technical Review Committee consisted of: David Erickson Ph.D., Centers for Disease Control, Atlanta, Georgia; Diana Petitti MD, MPH, University of California, San Francisco, Calif; Alice Whittemore Ph.D., Stanford University, Stanford, Calif; Warren Winkelstein MD, MPH, University of California, Berkeley, Calif; Dr. Kenneth Rothman D.D.s. Dr. PH., Univerity of Massachusetts, Worchester.

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Without the assistance of those mentioned, and the cooperation of the families who participated, their physicians and the staff of the medical records room these studies would not have been possible.

CARDIAC DEFECTS IN RELATION TO WATER CONTAMINATION, 1981-1982, SANTA CLARA COUNTY, CALIFORNIA

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CARDIAC DEFECTS IN RELATION TO WATER CONTAMINATION, 1981-1982, SANTA CLARA COUNTY, CALIFORNIA

ABSTRACT

In 1981 a leak of solvents from an underground storage tank was detected at the Fairchild Camera Company, an electronics manufacturing company in Santa Clara County. Solvents were then found in a well supplying water to the nearby community. Residents became concerned about a possible relationship between adverse reproductive outcomes and consumption of contaminated water. One resident wrote to the president of the Great Oaks Water Company (GOWC), of which Well #13 is a part, reporting nine cases which included several spontaneous abortions and birth defects. To investigate this issue the California Department of Health Services (CDHS) conducted two epidemiological studies: one, an examination of pregnancy outcomes; the other, which is reported here, a countywide study of major cardiac defects. This study, which compares rates of cardiac defects in the area served by the Great Oaks Water Company with rates in the rest of the county finds an excess of major cardiac defects in the service area of the Great Oaks Water Company. In 1981, ten babies with major cardiac defects were born to residents of this district. This represents an excess of six cases over the number expected in this period based on rates in the remainder of the county (relative risk estimate 2.6, significance probability 0.01). Available data suggest that this problem was limited to 1981. The distribution of cases throughout the county suggests that an excess of cardiac cases also exists in several of the census tracts surrounding the study area. A comparison of the distributions of the cardiac defect cases in time and space with the distribution patterns of the water supply and contaminants suggests

that the December 1981 solvent leak is an unlikely explanation for this excess. Other possible explanations are discussed.

SUMMARY

BACKGROUND AND METHODS

On November 17, 1981, a leak of toxic chemicals was discovered near an underground waste solvent storage tank at the Fairchild Camera and Instrument Company in San Jose, California. This tank was located about 2,000 feet from a well (Well #13) which supplied drinking water to the nearby industrial and residential areas. On December 7, this well was removed from service. At that time 1,1,1-trichloroethane (TCA) was found at this well at 1,700 ppb. On December 14, TCA levels reached 8,800 ppb. Following the notification of this contamination the community expressed concern about the possible health effects of this exposure. In response to this concern the Health Officer of Santa Clara County convened a meeting of an advisory committee and CDHS staff to discuss the problem and to consider alternative ways to evaluate the health risks of this exposure.

CDHS staff reviewed the scientific literature but found no human epidemiologic studies which discussed the reproductive effects of these chemicals. Data from animal studies did not suggest any effects of these chemicals on reproduction. Similarly, analysis of birth certificates did not indicate an excess of adverse pregnancy outcomes in the GOWC service area compared with the county as a whole. Nevertheless, it is well known that birth certificates cannot be used to rule out increases in rates of birth defects because they under-report such defects. Furthermore, vital records provide no data on spontaneous abortions.

Anecdotal reports suggested an excess of spontaneous abortions and cardiac defects in the area near Well #13 (Los Paseos), and it was agreed that CDHS would conduct two studies to address these concerns.

One of these, an interview study on all pregnancy outcomes, is reported separately. The cardiac defect study was designed to meet the following objectives.

1) To determine whether the cluster of cardiac defects cases which had been reported in and around the Los Paseos community represented a rate which was higher than expected;

2) To determine whether an excess could be explained by maternal risk factors;

3) To determine whether an excess could be attributed to any environmental risk factors and, in particular, to the leak identified in December 1981 at the Fairchild plant.

The cardiac defect study is based on data collected through a review of hospital records. Hospital records were searched for all cases of cardiac defects among residents of Santa Clara County born in 1981 and 1982. In order to qualify as a case, a baby had to have a major cardiac defect diagnosed in hospital by one year of age. Because the contaminated well was removed from service on December 7, 1981, it is highly unlikely that babies born after September 1, 1982, were exposed to this source. Since the study attempted to compare rates during the period when TCA was most likely to be in the drinking water, births after September 1982 were not included in this study.

The initial contamination was identified in a well in the Great Oaks Water Company. Because the entire service area was potentially exposed and the entire service area of this water company coincided almost exactly with census tract boundaries, it was selected as the study area.

A verbatim record of all diagnoses was obtained as well as information on the precision of the diagnoses, method of confirmation, chromosomal defects, family history of heart disease and maternal diabetes. The census tract for residence at birth was identified for each case, and rates of cardiac defects were computed for each census tract in the county. Rates for all residents in the study area were compared with rates for residents in the remainder of Santa Clara County. In addition, rates in the Los Paseos community (CT5120.12), a census tract close to Well #13, were compared with county rates (excluding the study area).

RESULTS AND CONCLUSIONS

The entire study area, and the Los Paseos community in particular, showed an excess of major cardiac defects. This excess was confined to cases born in 1981, but the lack of a full year of follow-up in which to identify all cases, makes conclusions about 1982 less certain. The relative risk estimate for all 1981 major cases in the study area, compared with the rest of the county, was 2.6 with a 95% confidence interval of 1.3 to 4.9. Removing Down's syndrome cases or cases with a family history of heart disease from the analysis had little effect on these results. There is no discernable pattern in the diagnoses of cases in the study area, nor was there an excess of babies falling into other diagnostic categories such as simple patent ductus arteriosus or arrhythmia. A review of the geographical distribution of cases throughout the county suggests that a similar excess exists in census tracts surrounding the study area.

An analysis of the distribution of water throughout the study area indicates that the leak of chemicals into Well #13 is unlikely to explain this excess. In particular, GOWC operated eleven other wells, all of which were active during the study period, which makes it highly unlikely that water from Well #13 was distributed throughout the entire GOWC service area. Since the addresses at birth of nine of the twelve cases served by GOWC were located in the northern and western portions of the service area, whereas Well #13 is located in the southeast, it is unlikely that these nine cases had been exposed to this source of contamination. In addition, the birth dates for the major cardiac cases occur fairly uniformly throughout 1981 with the rate of cardiac defects decreasing in the second half of 1981 and early 1982. No cases were identified among babies born in the study area after April 1982. Although the onset of the leak was uncertain, we know that there was definite contamination in Well #13 in December 1981 and for some indefinite period before that time. There are no cases among births who were conceived at that time. Thus, the distribution of cases in time does not support a conclusion that the Fairchild leak was the cause of the observed excess.

Other explanations must be considered. First, it is known that congenital cardiac defects can result from maternal rubella. However, a review of infectious disease records showed no excess in reporting of this disease in the study period. The possibility of some other unrecognized infectious teratogen is a theoretical possibility which cannot be ruled out. Other possible environmental factors were considered. A second, smaller leak of TCA which occurred in 1980-81 at IBM Corporation is unlikely to explain these cases because of its location and the low level of contamination. The service area of the water company studied contains fifteen smaller companies, several of which use chemicals similar to those used at the Fairchild and IBM plants. Although there is no indication of water contamination from these industrial sites, air contamination cannot be ruled out. Unfortunately, ambient air data during the study period are not available. Malathion spraying was considered as a possible explanation. However, spraying did not begin in the GOWC service area until August 1981. Therefore, this exposure could not be related to an excess of cases in 1981.

In terms of the stated objectives of the study the conclusions are as follows:

1) The cluster of cardiac defect cases which had been reported represents an increase in rates in the study area which exceeds what would be expected on the basis of rates in the remainder of the county or from reports in the scientific literature. The increase appears to be limited to 1981. The distribution of cases suggests that this increase was also seen in adjacent census tracts served by other water companies.

2) Maternal risk factors for congenital heart defects are few. The factors that were examined do not explain the observed increase in rates.

3) This investigation has not identified any environmental factor responsible for the increased rates of cardiac defects. In particular, the time and geographic pattern of cases makes the contamination of Well #13 by the Fairchild leak an unlikely explanation.

INTRODUCTION

1. History of the Problem

On November 17, 1981, a leak of toxic chemicals was discovered near an underground waste solvent storage tank at the Fairchild Camera and Instrument Company in San Jose, California. This tank was located about 2,000 feet from a well (Well #13) which supplied drinking water to the nearby industrial and residential areas. On December 7, Well #13 in the Great Oaks Water Company (GOWC), the well closest to this Fairchild plant, was removed from service. At that time, 1,1,1-trichloroethane (TCA) was found at this well at 1,700 ppb. On December 14 TCA was measured at 8,800 ppb. In March 1982 sampling also located 1,1-dichloroethylene (DCE) in Well #18 at 58 ppb and TCA and DCE at much lower levels in Well #8; this finding was related to a smaller leak at a nearby IBM plant. Well #8 was removed from service in March 1982. No contaminants were detected at any of the other eleven wells in the water district, except for low levels of freon 113 found in Well #2. For this reason, the latter well was also shut down in the spring of 1982. The location of these wells and companies are contained in Figures 1 and 2.

Following the notification of this contamination the community expressed concern about the possible health effects of this exposure. On January 27, 1982, one resident wrote to the president of GOWC reporting nine cases of adverse pregnancy outcomes in homes near Well #13. Among these were several spontaneous abortions and cardiac defects. On February 23, 1982, the Health Officer for Santa Clara County convened a meeting of an advisory committee (Santa Clara County Advisory Committee on Environmental

Teratology) and staff of CDHS to discuss the problem and to consider alternative ways to evaluate the health risks of this exposure.

2. Extent of the Problem

a) Review of Existing Epidemiologic Data

A review of available data did not indicate any excess in birth defects or an increase in the proportion of low-birth-weight babies in the GOWC service area. However, the only data available, before the CDHS studies were carried out, were derived from birth certificates. Since only about 20% of birth defects are reported on birth certificates, the absence of an excess of defects in the affected area was not convincing. Futhermore, since there is no reporting of spontaneous abortions on vital records, this outcome could not be evaluated. These data, prepared by Santa Clara County Health Department, are contained in Appendix A. No previous epidemiological studies on the possible adverse health effect of environmental exposures to TCA have been reported. There have been studies of workers with occupational exposure to TCA, but none of these mentioned reproductive effects. No clinical reports associate maternal exposure to TCA with congenital malformation in offspring (1).

b) Review of Animal Data

Data related to the possible reproductive effects of TCA in laboratory animals were also evaluated. The available data provide no evidence that TCA is teratogenic in laboratory mammals. Some fetotoxic and embryotoxic effects were evident at higher exposure levels, but these were attributed by the authors to maternal toxicity. No study reported an excess of cardiac malformations. However, it is possible that these abnormalities could be overlooked unless specifically identified as an outcome of interest; the size of the fetal and newborn heart in test animals makes the diagnosis of these defects difficult.

The conclusions of a toxicological review of DCE were similar. The toxicological literature on freon was also reviewed. Although little is known about the reproductive effects of this chemical, there does not appear to be cause for concern. Summaries of these animal studies on TCA and DCE and freon are contained in Appendix B.

c) Geographical Boundaries

The well at which contamination was first measured, Well #13, is one of twelve wells operated in December 1981 by GOWC.* The area served by GOWC is contained within seven census tracts listed in Table 1. In what follows, this area will be referred to as the study area.

Almost all private homes in these census tracts are served by GOWC. The exceptions are two mobile home parks, a few isolated single family dwellings and a small corner in the northwestern section of CT5120.02. The residences served by private wells are shown in Figure 3.

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* Well #16 began operation in June 1983.

In principle, water from any well in the system can be distributed to any home served by the Great Oaks Water Company. However, homes are most likely to receive water from the closest operating wells. Thus, water from Well #13 is unlikely to have reached all portions of the study area. Nonetheless, because the possibility exists that the entire region may have received this water, the entire Great Oaks service area was considered to be the study area for the purposes of this investigation.

d) Temporal Boundaries

Since Well #13 was removed from service on December 7, 1981, the end point of exposure from this source is fairly well defined.* Similarly, Well #8 was shut down in March 1982 after TCA was found there. However, the time at which exposure from the Fairchild leak began is less clear since no water sampling was done prior to December 1981. Fairchild Camera and Instrument Company did not maintain an ongoing materials balance report from which a beginning date for the leak into Well #13 could be estimated.

A materials balance report was reconstructed retrospectively by Fairchild Camera and Instrument Company working in cooperation with CDHS. However, as the report states, there is considerable uncertainty in the estimates which were derived. This report estimates the difference between solvent received and solvent disposed of and evaporated monthly from the time the plant began operation in January 1977. An accumulated difference is calculated which is assumed to be directly related to the amount of solvent leaked from the storage tank (Figure 4).

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* It is possible that, because of the high levels of TCA present, some TCA may have adhered to the pipes or stayed in pipes with low usage. Thus, TCA could have remained in the distribution system for as long as several weeks after the date of removal of Well #13 from service.

Contamination in Well #8 was not detected until 1982. However, leakage of TCA at low levels was reported by IBM Corporation to the Regional Water Quality Control Board beginning in October 1980.

Because of the uncertainty of the time of initial exposure it was decided to include all cases born in 1981 as potentially exposed. Since exposure to contaminants in Well #13 was unlikely after December 1981, and since this study compares heart defect rates in a study and comparison area during the period of most likely exposure, births occurring after September 1, 1982, are not included in these analyses.

e) Extent of Contamination

Levels of TCA in Well #13 increased from 1,700 ppb on December 7 to 5,700 ppb on December 10 and reached a high of 8,800 ppb on December 14. According to the Environmental Protection Agency(2) the "Suggested No Adverse Response Level" (SNARL) for noncancer effects of long-term exposure is 1,000 ppb, although the taste and odor threshhold is 300 ppb.

Detectable levels of TCA were first found in Well #8 on March 19, 1982. These levels were considerably lower than those obtained at Well #13 and never exceeded 33.5 ppb in the Great Oaks wells. However, TCA was measured at 250 ppb in off-site monitoring wells near the IBM plant. Dichloroethylene was found at 88 ppb in Well #13 and 9.6 ppb in Well #8. This should be compared to the EPA SNARL for noncancer effects of long term exposure of 100 ppb(2). In addition, freon 113 was measured at 38 ppb in Well #13 and at 8 ppb in Well #2. No SNARL exists for this compound, but there is an occupational guideline (Threshhold Limit Value) of 1000 ppb in the ambient air of the workplace on a 40 hr/week basis.

There were several chemicals which were present in the waste storage tank at Fairchild but which were found in only negligible amounts in Well #13. These include acetone, xylene and isopropyl alcohol.

A large number of pollutants were looked for and were not detected. As an example, a report from one such priority pollutant analysis for Well #13 is attached. (Appendix C)

3. Response to the Problem

On March 17, 1982, the Advisory Committee agreed that an epidemiological study on reproductive outcomes should be carried out in the area where contamination may have occurred. The study design initially selected by the committee was an interview study of reproductive outcomes in of the Los Paseos area (CT5120.12) and a comparable control census tract outside the area served by GOWC (CT5120.08). Initial fieldwork on the interview study began in November 1982.

At that time it was apparent that the interview study would not have sufficient numbers of subjects to be informative about a possible excess of cardiac defects. In fact, assuming that major cardiac defects occur at the rate of 3 per 1000 live births, this interview study could not detect a tenfold increase in risk of major cardiac malformations.* Therefore, it was decided to carry out a separate study designed specifically to investigate cardiac defects. This latter study, because it compares births in a seven census tract study area to the rest of the county, had adequate numbers to detect a two to three fold increase.

The cardiac study was designed to meet the following objectives:

1) To determine whether the cluster of cardiac defects cases which had been reported in and around the Los Paseos community represented a rate which was higher than expected;

2) To determine whether any excess can be explained by maternal risk factors;

3) To determine whether this excess can be attributed to any environmental risk factors and, in particular, to the leak indentfied in December 1981 at the Fairchild plant.

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*Using a two-tailed test at a significance level of 0.05 with power of 80%.

The cardiac defect study is based on data collected through a review of hospital records. Hospital records were searched for all cases of cardiac defects among residents of Santa Clara County born in 1981 and 1982. In order to qualify as a case, a baby had to have a major cardiac defect diagnosed in hospital by one year of age.

A verbatim record of all diagnoses was obtained as well as information on the precision of the diagnoses, method of confirmation, chromosomal defects, maternal diabetes and family history of heart disease. The census tract for residence at birth was identified for each case and rates of cardiac defects were computed for each census tract in the county. Rates for births in the study area were compared with rates for births in the remainder of Santa Clara County. In addition, rates in the Los Paseos community (CT5120.12), a census tract close to Well #13, were compared with county rates (excluding the study area).

Ascertainment of heart defects was carried out throughout Santa Clara County for all births in a two-year period(1981-82). Relevant data items which are usually available on hospital charts were abstracted. These are contained in the attached data collection form (Figure 5A-B).

A pilot study to test data collection procedures was begun in April 1983 in the office of a pediatric cardiologist in Santa Clara County. Subsequently, case ascertainment began in hospitals in May 1983.

METHODS

The procedures for case ascertainment, chart abstraction and classification of cases are discussed. A flow diagram outlining these procedures is attached (Figure 6).

I. Case Ascertainment

Staff of the Birth Defects Monitoring Program (BDMP) of the CDHS ascertained cases using a discharge diagnostic index at each of the eleven hospitals in the Santa Clara County as well as at the California Children's Service and the major out-of-county referral hospital for childhood cardiac disease. These hospitals, together with the number of cases ascertained at each, are listed in Table 2. In order to minimize the chance of overlooking any possible cardiac defect cases, charts were obtained for all children with a discharge diagnosis code in 1981-82 of:

- o cardiac malformations (ICD9 745-747.9),
- o cardiovascular disease (ICD9 390-459).

Charts were abstracted for all potential cases that satisfied the age and residence requirements of the study as follows:

- o Residence in Santa Clara County at birth,
- o Birth date in 1981-1982,

- Diagnosis of a cardiac defect in a child under one year of age in a Santa Clara hospital, California Children's Service or University of California San Francisco Hospital.

2. Chart Abstraction

CDHS staff, under the supervision of BDMP, abstracted hospital records for all potential cases. After excluding records which did not meet the age and residence requirements, a total of 781 charts were abstracted.

All relevant diagnoses were recorded verbatim along with the method of confirmation (e.g., echocardiogram, catheterization), precision of diagnosis ("probable", "rule out", etc.) and specialty of diagnosing physician, if available. All surgeries, any syndromes of which congenital heart disease is a part, and any mention of a history of heart disease in the immediate family or maternal diabetes were noted.

3. Coding and Disease Classification

Cases were classified as "Major", "Other Diagnostic Categories", and "Diagnosis Uncertain." Babies without evidence of any heart defect were excluded. The classification of all cases abstracted is contained in Table 3. The definition of these categories follows.

a) Major Cases

All cases with a definite diagnosis of a cardiac anomaly, other than those listed below under "Other Diagnostic Categories", were considered to be major cases. The range of diagnoses in these major cases and their frequencies are contained in Table 5. Major diagnoses, one or more of which were present for each major case, are listed in Table 6. Analyses were carried out both with and without the seven cases of patent ductus arteriosus (PDA) in full-term infants.

Most major cases were ascertained at more than one hospital. Records were combined and all diagnoses for a single child were reviewed by one of the investigators. When diagnoses were incomplete or conflicting, an attempt was made to contact the diagnosing physician. Because this was not always possible, and problem cases remained, we asked six pediatric cardiologists in the county to review these unresolved cases. If it could not be decided whether or not the child was a major cardiac case, the case was categorized as "Diagnosis Uncertain" and excluded from further analyses. Three cases were excluded because of uncertain diagnosis. None was living in the study area at birth.

b) Other Diagnostic Categories

Cases with the following diagnoses and without other accompanying complications, such as congestive heart failure, were considered to fall into "Other Diagnostic Categories" (ODC). These cases fell into one of the following categories:

- o ventricular septal defect (VSD) or atrial septal defect (ASD),
- o patent ductus arteriosus (PDA) in a premature infant,
- o arrhythmia and/or functional murmur.

While the decision to ascertain cases which fall into the latter two diagnostic categories may be debatable, we include them here for completeness.

c) Nonheart defects

Because of the wide range of diagnoses ascertained, a large number of charts were reviewed for children with diagnoses of cardiovascular disease but with no cardiac anomaly. These included such diagnoses as: single umbilical artery, cardiac arrest and pulmonic hypertension. These 117 cases were excluded from further analysis.

4. Assignment of Cases to Census Tracts

Census tracts at birth were identified for all cases. Initially, census tracts were identified from the state vital statistics records. When the census tract corresponding to the address obtained from hospital records was in disagreement with this computer file, the hard copy of the birth certificate was retrieved and the address corrected. Several sources were used to update the census tract information contained in the vital statistics records. These details are contained in a recent CDHS study(3).

In addition, the longitude and latitude of address at birth was computerized for each major case in order to display the distribution of these cases graphically.

5. Exposure Definition

a) Geographical Definition

Initially, it was assumed that the boundaries of the study area coincided with census tract boundaries and included census tracts 5120.02, 5120.07 and 5120.09-5120.13 (Figure 2). We subsequently asked the GOWC to identify cases served by their company. All cases residing in these tracts were served by GOWC. However, not all private homes in CT5120.02 and CT5120.07 are served by the GOWC. In order to calculate census tract specific rates among homes served by GOWC it was necessary to estimate the proportion of live births living in residences served by GOWC.

For this purpose, we selected a sample of random births using computerized birth certificates. Fifty babies were selected from CT5120.02 and fifty from CT5120.07. The addresses at birth for these one hundred babies were reviewed by GOWC. Based on these samples we estimated that 96% of CT5120.02 and 94% of CT5120.07 are served by GOWC. These percents are contained in Table 1. Numbers of live births in subsequent calculations are based on these percents applied to all live births in these tracts.

b) Temporal Definition

As discussed above, the precise onset of the exposure period is unknown. However, it is known that Well #13 was taken out of service on December 7, 1981. Since the period from day 20 to day 50 of gestation is considered the most critical for cardiac development (4), a child born after August 1982 would be unlikely to have been at risk of a cardiac malformation due to exposure from this source. To allow for possible errors in dates, and residual contamination in the water system for a short time after December 7, we included cases born before September 1, 1982 in the analysis. The period January 1, 1982 to September 1, 1982 is referred to as 1982A. Rates have been calculated for the period 1981-82A as well as for 1981 alone. Table 4 contains counts of cases analyzed.

6. Estimating the Extent of Incomplete Ascertainment of 1982 Cases

By definition, a child is included as a case if diagnosed as having a cardiac defect up until one year after birth. For example, a child born September 1, 1982, would be counted as a case if hospitalized with a cardiac defect on, or before, September 1, 1983. Case ascertainment began in May 1983 and ended November 1983. At that time, it was not possible to ascertain cases diagnosed in 1983 completely because the hospital discharge indices were not available. Thus, a child born in 1982 who was not diagnosed until 1983 would not have been ascertained. To estimate the extent of this problem we calculated the percentage of cases which would have been missed among the cohort born in 1981 had we not been able to ascertain cases in 1982. In addition, we compared the rates of defects in the county (excluding GOWC service area) in 1981 and 1982. It is our intention to complete this ascertainment when possible. However, we feel that the 1981 data are more appropriate for analysis at this time. Thus, all analyses are presented for 1981 alone. Data for the time period January 1, 1981, through September 1, 1982, are included for completeness.

7. Comparison Census Tracts:

Santa Clara County Health Department (SCCHD) staff used 1980 census data to compare the socio-economic characteristics of census tracts within the county. At the time this analysis was undertaken, SCCHD was interested in identifying census tracts that were most similar to CT5120.12, the study census tract for the interview study. This census tract is referred to as Los Paseos. SCCHD identified 7 census tracts as being most similar to Los Paseos with respect to such variables as: total population, ethnic distribution, median housing cost and birth rate. None of these variables are known to be related to the risk of cardiac malformations (5). Nonetheless, a comparison of cases in the study area to cases in these seven tracts was carried out; this analysis is discussed in Appendix D.

8. Random Sample of all Santa Clara County Births

A random sample of 130 births was selected from the computer files of live births for 1981-82 to correspond in number to the 130 major cases. Birth date and address at time of birth were obtained from hard copies of the birth certificate in order to compare the spatial distribution of major cases to the distribution of this sample. This comparison is discussed in Appendix E.

9. Cases Identified through Physicians' Offices

Some proportion of significant cardiac malformations will not result in a hospital discharge diagnosis within the first year of life. This will occur either when the defect is diagnosed in a physicians' office during this period but hospitalization occurs after the first year or when the first diagnosis at any source occurs after the first year. In the latter situation it is not possible to determine the magnitude of underascertainment until several years have elapsed. In the former situation it is possible to estimate the number of cases missed. This was done in the following way. All records of one of the six pediatric cardiologists in Santa Clara County were reviewed. Cases ascertained through this source were compared to those identified through hospital records. In this way we could estimate the proportion of children who were diagnosed as having a cardiac malformation during the first year of life in a pediatric cardiologist's office but who were not hospitalized for that defect nor received a diagnosis at birth of a cardiac defect.

10. Analysis

Rates of major cardiac defects in the study area were calculated for 1981 alone as well as for 1981-82A. These rates were compared to those for the remainder of the county. These comparisons were repeated excluding cases with Down's syndrome as well as cases with family history of heart disease. This latter exclusion is somewhat questionable since family history was noted irregularly on hospital records. Furthermore, it may be precisely those children with a family history of cardiac disease who are most sensitive to a prenatal exposure.

Rates were compared using Fisher's exact test, and 95% confidence limits were obtained. Confidence limits were calculated using the method of Cornfield (without continuity correction). This procedure has been shown to produce uniformly valid intervals and is considerably simpler than the exact method (6).* All significance probabilities are one-sided. Similar comparisons were carried out for the single census tract known as Los Paseos.

RESULTS

The results for 1981 and January 1, 1981, to September 1, 1982, will be reported separately. Results will be given for all major cases, as well as for major cases excluding cases of Down's syndrome and any case in which there was a history of heart disease in the immediate family. In each of these categories several comparisons have been made: 1) the Los Paseos area (CT 5120.12) has been compared to the entire county of Santa Clara, excluding the area served by the Great Oaks Water Company and; 2) each of these comparisons has been made for the larger study area. In addition, the distribution of cases in time and space will be discussed as well as the distribution of diagnoses for major cases. Finally, an estimate of the sources and extent of underascertainment will be presented. All rates are given in terms of cases per 1000 live births.

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* Confidence intervals were calculated using Program 23 in Rothman and Boice (7) adapted to eliminate the continuity correction.

1. Major Cases Born in 1981

In 1981 there were two cases of major cardiac defects in the Los Paseos area yielding a rate of 15.15/1000. Although based on only two cases this rate was considerably higher than the rate for the county excluding GOWD, 3.11/1000. The relative risk estimate for this comparison is 4.9 with a 95% confidence interval of (1.3, 18.5). When the five cases of PDA in a term infant are removed from the numerator of the rate for the rest of the county, the relative risk estimate for Los Paseos increases to 5.1.

The relative risk estimates comparing the entire study area with the county (excluding GOWD) is 2.6, with a 95% confidence interval of (1.3 to 4.9) and an exact significance probability of 0.01. (Without the PDA cases the relative risk estimate increases slightly to 2.7).

When chromosomal defects are excluded, the countywide rate for 1981 drops to 2.60/1000. The rate in Los Paseos remains unchanged at 15.15/1000 whereas the rate in the entire study area is slightly lower (7.10/10000). Therefore, the relative risk estimates and their confidence intervals are similar to those obtained for all major cases (See Table 7B).

Finally, when cases with family history of cardiac disease are excluded as well as Down's syndrome cases, the rate in the portion of the county used for comparison drops to 2.35/1000. The relative risk estimate comparing the study area with the balance of the county remains at 2.7 (Table 7C).

2. Major Cases Born in 1981-82A

Because of incomplete ascertainment of cases born in 1982 and because it is necessary to consider only part of this year as the possible exposure period, the results based on January 1, 1981, to September 1, 1982, are less reliable than those for 1981 alone. Nevertheless, we include them here for completeness. These results are contained in Tables 8A-C. The locations at birth of major cases born (1981-82A) in the study area are shown in Figure 8.

As expected, because of incomplete ascertainment, the countywide rates for 1981-82A were somewhat lower than those for 1981 alone. The relative risk estimates for the study areas are similar to those for 1981, though somewhat lower. Slightly increased relative risk estimates are obtained when Down's syndrome cases are excluded. Excluding the PDAs in term babies also increases the relative risk estimate slightly to 2.2.

3. Diagnoses of Major Cases

Diagnoses of all major cases in the county are contained in Table 5A together with the percent distribution. This table includes minor defects, such as VSD, only when a significant diagnosis, such as tetralogy of Fallot, was also present. A listing of these major diagnoses is contained in Table 5B. In order to qualify as a major case, a child must have had at least one of these diagnoses. Major cases in these analyses include seven cases of PDA in a full-term infant without any of the diagnoses in Table 5B. However,the results of removing these seven cases has been discussed and shown to be minimal. The distribution for major cases in GOWD is also given in Table 6A (None of these were cases of PDAs without other major diagnoses). As can be seen by comparing these two distributions, the cases in the study area appear to differ little in diagnoses from those in the county as a whole. However, cases in that area on the average, somewhat more complex; these cases averaged 3.3 diagnoses per case compared to 2.5 diagnoses per case for the county as a whole.

4. Distribution of Major Cases in Time and Space

A plot of the twelve major cases which occurred in the study area does not indicate an unusual geographical clustering within this area (Figures 7 and 8). One or more cases are found in each of the seven census tracts in GOWC except CT5120.10. Since the numbers of live births in these census tracts do not differ widely (ranging from 209 to 445) this is not different from expected. In particular, the excess is not confined to the tract containing Well #13 (CT5120.11) or the Los Paseos area (CT5120.12). The geographical distribution of major cases throughout the county was also considered. As can be seen in Figure E-3 an excess of cardiac cases can

also be seen in census tracts surrounding the study area. These tracts received water from a different water company.

The distribution in time of the twelve major cases in the study area was considered (See Table 10). Seven of these cases were born, at the rate of approximately one a month (two in June 1981), in the first half of 1981, and only two cases born in 1982; these occurred in April. If any trend can be discerned, it is a decrease in prevalence over the exposure period studied. Any exposure which was causally related to these cardiac defects should have been present during the 20-50th day of gestation, or as early as April 1980 for cases born January 1981. If such an exposure were the result of ground water contamination following a leak of toxic substances, that leak should have occurred in March 1980 (because of the time necessary for such contamination to reach the ground water). Thus, the pattern of contamination most consistent with these birth dates would have been at a maximum in March to August 1980 and would have tapered off after that time. This picture is not consistent with the only data available on the pattern of contamination at Fairchild as contained in the materials balance report. This latter report suggests an increase in leakage until a maximum was reached in December 1981. It should be noted, however, that the materials balance report was reconstructed retrospectively by Fairchild Company and, as they indicate, is subject to considerable error.

It appears that the excess of cardiac defects in the study area may be confined to 1981 because of the absence of cases after April 1982 in the available data. However, further study is necessary to confirm this.

5. Other Diagnostic Categories

A total of 240 children fell into Other Diagnostic Categories. Of these,

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* Further ascertainment of cases born in 1982 may increase this number somewhat. However, only a 12% underascertainment is estimated. An additional 6 cases (corresponding to 75% underascertainment) would be necessary if the rates in 1982A were to be similar to 1981 rates.

211 were born in 1981-82A, yielding a rate of 5.99/1000, only somewhat less than the 1981 rate of 6.22/1000. As can be seen in Tables 9A-B there was no excess of these cases in the study area for either time period. Relative risk estimates ranged from 0.81 - 1.51.

The distribution of diagnoses among the eleven ODC children born in the study area was not unusual. There were 4 cases of PDA, 4 of VSD and 3 cases of arrhythmia. This is similar in distribution to the 27%, 39% and 34% of diagnoses among all children in these categories shown in Table 6. Thus, there was nothing remarkable in either the number or diagnoses of these ODC children seen in the study area.

6. Comparison of Cardiac Defects in Two Pregnancy Outcome Studies Conducted by CDHS

The time periods and geographic areas included in the two studies carried out concurrently by CDHS in Santa Clara County were overlapped. It is of interest to compare the degree of agreement in cardiac cases identified in these two studies within the common time period and geographic areas.

a) Cases Identified in Cardiac Study

There were two major cases identified in the cardiac study in each of CT5120.08 and CT5120.12, the two census tracts included in the interview study. Of these, all but one were identified in the interview study as well. This last case was not included in the study because the family had moved between the census and interview and was not available for interview. This child's record was reviewed but there was no mention of a defect at birth. Therefore, this child did not satisfy the definition of a case in the interview study.

There were no cases in Other Diagnostic Categories in CT5120.12. There was a single possible case in CT120.08 ("probable PDA in a premature infant"). This defect was not mentioned by the mother at the time of interview so that this child was not included as a birth defect in the interview study.

b) Cases Identified in Interview Study

There were no major cases identified in the interview study which had not been included in the cardiac study.

The interview study identified one child in each of CT5120.08 and CT5120.12 with a defect who were not included in the cardiac study. One of these, the case in CT5120.12, was an atrial septal defect in a child with Down's syndrome. This child would have been counted among "Other Diagnostic Categories" except that the diagnosis was made after one year of age. The second child, residing in CT5120.08, had an atrial septal defect which was not present in the hospital record. Therefore, neither of these children met the definition for inclusion in the cardiac study.

7. Cases Initially Identified by the Community

In the letter of January 27, 1982, written by a concerned citizen to GOWC, nine problem pregnancies were identified. Of these, three were cardiac defects. Two of these cases were born in 1981 and are included in the study. The third, born in 1979, was not. One of these is in CT5120.11 and one in CT5120.12.

The question of whether or not to include these two "index cases" in the analysis is controversial. Clearly, the exclusion of these cases leads to a lower estimate of relative risk and wider confidence limits for this estimate. If this is done, for example for 1981, the relative risk estimate for the study area, relative to the remainder of the county, drops from 2.55 to 2.04 (p=.056). It is apparent that the observed excess for 1981 is not entirely the result of a small cluster of index cases.

8. Sources of Errors in Ascertainment and Classification

While considerable effort was spent to locate and correctly classify every case, several sources of potential errors in ascertainment and classification are recognized. A discussion of these follows.

a) Movement of Cases between Exposed and Unexposed Area

Addresses at birth were used to locate all cases geographically. In fact, if an address had been available for the mother during her early pregnancy this would be a more accurate means of classifying cases with respect to exposure. An error in classification would have occurred whenever a case was counted among in the study area cases but the mother moved into the area late in pregnancy or conversely. In fact, any cases who were Santa Clara residents while in utero, but whose mother moved outside the county before birth, would be missed.

In addition, children born in Santa Clara County who moved out of county and had a defect diagnosed later would be missed. The extent of this underascertainment is difficult to estimate.

b) Cases Born in 1982 with Defects Diagnosed in 1983

As discussed above, because ascertainment was carried out in 1983, children first diagnosed in 1983 would not have been ascertained. By calculating the percent of 1981 cases who were not diagnosed until 1982 it is possible to estimate the degree of underascertainment due to this source. Using this method, it is estimated that there has been a 17% underascertainment of 1982 cases and an underascertainment of 1982A cases of 12%. The first of these is also the estimate provided by a comparison of 1981 and 1982 rates of major cases throughout the county.

c) Cases First Diagnosed in Hospital after One Year of Age

We were not able to estimate the degree of underascertainment resulting from the requirement that cases be diagnosed in a hospital before the first birthday. However, in a large follow-up study of 16,503 live births it was reported that 14% of congenital heart disease which was detected through routine care by five years of age was not diagnosed at one year(7).

d) Cases Diagnosed by a Pediatric Cardiologist by One Year of Age

In order to estimate the extent of this source of underascertainment we reviewed the records of one pediatric cardiologist in Santa Clara County. Of the twelve definite major cases ascertained in this office which satisfied the study criteria, all but four were also ascertained in one or more hospitals in the course of this study. The reasons for missing these four cases are as follows:

(1) There were two cases who were born in 1982 and hospitalized first in 1983 while still less than one year of age. These cases will most probably be identified when 1982 ascertainment is completed.

(2) There were two cases who were not included because they were not hospitalized by one year of age. The cardiologist expects that surgery will be required at a later date for both of these children.

Therefore, we estimate that restricting ascertainment to hospitalizations by one year of age resulted in an underascertainment of 2 out of 12 or 17%. This estimate assumes that the first two cases will be identified through hospital records when 1982 ascertainment is completed.

e) Cases not Ascertained through Discharge Summaries

Ascertainment for this study was carried out through a review of summaries of discharge diagnoses (referred to as the discharge index, or DI). It is possible, though unusual, that cardiac defects which are not on these summaries are identified through other sources of ascertainment. Using results from a recent study of completeness and accuracy of alternative sources of ascertainment of birth defects, carried out by CDHS, the extent of this underascertainment can be estimated (9). In that study, carried out in Humboldt and Del Norte Counties (1976 - 1981), 22 cases of major cardiac defects were identified using all sources. Of these, only one (4.5%) had no cardiac defect listed on the discharge summary of any hospital in the study area or at CCS. This case was identified through the logs of the Intensive Care Nursery, which listed other non-cardiac defects for this child.

9. Comparison with Rates of Cardiac Defects Reported in the Literature

This study found a total of 130 cases of major cardiac defects in the entire Santa Clara County. In addition, there were 240 children with other cardiac-related diagnoses which were anayzed separately. The overall rate of all cardiac cases falling in these categories, for Santa Clara County excludingthe study area was 9.4/1000 for 1981 and 8.9/1000 for

1981-82A. When murmurs and arrhythmias are excluded, these rates drop to 7.3/1000 and 7.0/1000 respectively. Finally, when all cases of Patent Ductus Arteriosus (PDA) are excluded, the rates are 5.0/1000 and 5.2/1000 for 1981 and 1981-82A.

This is somewhat lower than the rate of 7.8/1000 found by Hoffman et al (8) for cardiac defects, excluding arrythmias and PDAs, diagnosed by one year of age. However, this latter rate included outpatient cases without hospitalization. This was also the criterion used in the Collaborative Study (10) which found a rate of 8.1/1000 including isolated PDA. A rate of 5.8/1000, similar to that found in the present study, was reported by Neil (5). Finally, a British study by Bound and Logan which also included isolated PDAs reported a rate of 6.0/1000 (11). The latter study noted that 82 percent of the cases they included were recognized by one year of age.

Thus, the rates observed in Santa Clara County, excluding the study area, are similar to what would be expected based on the available literature while the rates in the study area are higher than expected. In this area in 1981, the rate of all cases, excluding PDA's and arrhythmias, was 10.3/1000.

DISCUSSION

Before December 1981, levels of toxics in either air or water in the study area were unknown. In the winter of 1981, high levels of TCA (1,700 ppb - 8,800 ppb) were measured at Well #13 in the Great Oaks Water Company following a leak at Fairchild Camera and Instrument Company. DCE was also found in March 1982 at 8.8 ppb at the same well. Also, TCA at 33.5 ppb as well as 9.6 ppb of DCE were measured at Well #8 as a result of a leak at a nearby IBM plant.

There were twelve wells operating in GOWC on December 1981. An evaluation of the water system's distribution system and operational procedures indicates that only localized areas would be expected to receive contaminated water prior to the detection of the contamination and the subsequent removal of the wells from service. Under normal operating conditions the majority of water from Well #13 was used by the Fairchild facility. The balance of water was supplied to the residential areas in CT5120.11 and CT5120.12. There is no indication that water from Well #13 was distributed throughout the entire system. A second important water source for Los Paseos (CT5120.12) was Well # 7, which is quite a bit closer to Los Paseos than Well #13 (See Figure 2). No contamination is found at Well #7. Extensive computer modeling and hydraulic analysis would be needed to determine the possible distribution of the contaminants in the water system under specific operational conditions when the wells were in service. However, pumping records indicate that during 1980-81 there was no month during which any of the wells in GOWC wells stopped pumping (Appendix F). Thus, it is unlikely that Well #13 was the source of water for the census tracts in which nine of the twelve major cardiac cases were born. However, it is a possible water source for CT5120.11 and CT5120.12 in which three cases were identified.

In summary, it is unlikely that the Fairchild leak identified in December 1981 could account for the excess of cardiac cases observed in the study area for the following reasons:

1) While three cases were born near the Fairchild plant and may have been supplied by Well #13, the remaining nine cases with addresses at birth in the north and west of the district most probably had other water sources. As discussed above, because of the large number of active wells in the mid- and northwest portion of the district, and the presence of excess cases immediately to the north of the district it is unlikely that water from Well #13, in the southeast, would have been a source of water for families these addresses.

2) While the time of onset of the Fairchild leak is unknown, the only available data suggest that the excess of solvents increased some time before the leak was detected in December 1981. If this leak were the source of contamination responsible for this excess of cardiac cases one would expect to see an increasing incidence of cases beginning in the second half of 1981 and extending into the summer of 1982. Because of incomplete ascertainment of 1982 cases, we cannot rule out the possibility that several more cardiac cases occurred in babies born in the 1982 study area that were not identified, but as of this time, ten of the twelve GOWD cases occurred in 1981 at the rate of approximately one per month and none occurred after April 1982. Thus, there is no indication of an accumulation of cases such as one would expect with an increasing rate of contamination.

Other explanations must be considered. First, it is known that congenital cardiac defects can result from maternal rubella. However, a review of infectious disease records showed no excess in reporting of this disease in the study period. The possibility of some other unrecognized infectious teratogen is a theoretical possibility which cannot be ruled out. Other possible environmental factors were considered. A second, smaller leak of TCA which occurred in 1980-81 at IBM Corporation is unlikely to explain these cases because of its location and the low level of contamination. The service area of the water company studied contains fifteen smaller companies several of which use chemicals similar to those used at the Fairchild and IBM plants. Although there is no indication of water contamination from these industrial sites, air contamination cannot be ruled out. Unfortunately, ambient air data during the study period are not available.

It is possible that other, undetected, leaks occurred at the Fairchild plant prior to December 1981. However, these, too, would have contaminated only Well #13, and thus, would not explain the nine north and northwest portion of the GOWC service area. The lesser leak at IBM was also considered. The first indication of such a leak was reported to the Regional Water Quality Control Board in 1980. However, the levels of contamination never exceeded the state action levels and were always very much lower than those found in Well #13. Moreover, the five major cases with residences in CT5120.02 and 5120.13 were unlikely to have received water from Well #8 because of the availability of two active nearby wells in CT5120.02.

It is possible that undetected contamination of water existed prior to December 1981. There were compounds used at Fairchild and probably at other industrial sites which would not have been detected by the usual testing protocols. For example, glycol ether, a spermatocide, was used at low levels by Fairchild and possibly by other companies. This substance would not have been detected in the water by any of the tests that were performed. Malathion spraying was considered as a possible explanation of these results. However, spraying did not occur anywhere in Santa Clara County until July 1981, and the GOWC service area was not sprayed until August 1981. Children in their second prenatal month at that time were born in March 1982. Thus, this factor could not account for the excess of cases observed in 1981.

Finally, it is necessary to consider the factors of chance variability and problems of bias. The results presented here are not likely to have occurred by chance, but the possibility of a false positive result can never be entirely ruled out. In addition, the diagnoses of cases in the study area do not aggregate so as to suggest a common etiology. Furthermore, the data are not consistent with the hypothesis that was being tested; no clustering in space and time, which would suggest a causal connection to the Fairchild leak was observed.

Because of the study design employed, very little individual data are available on these cases, and the potential for confounding by such factors as occupation cannot be estimated. However, data from the pregnancy outcome study demonstrate that variables which might predict negative pregnancy outcomes such as smoking, alcohol consumption and prior pregnancy loss were less prevalent in the Los Paseos area than the control area outside the study area. Furthermore, such factors have not been shown to be risk factors for cardiac malformations.

One strength of this study lies in the uniform and unbiased nature of case ascertainment. Medical records abstractors were unaware of the geographical location of the cases they were abstracting. This was also true until very late in the analysis when census tracting was complete, of the data analysis staff. Furthermore, the fact that there is no excess of children in Other Diagnostic Categories in GOWD, coupled with an excess of major cases, decreases the likelihood that reporting or diagnostic biases were present.

Finally, this study should be reviewed in conjunction with the pregnancy outcome study conducted concurrently by CDHS. This latter study demonstrates a significant excess of spontaneous abortions and birth defects and a deficit of low birth-weight babies in the Los Paseos (CT120.12) area as compared to a control area outside GOWD (CT120.08). Because the pregnancy outcome study was an interview study, very detailed information was obtained on a large number of confounders and extensive validation efforts minimized the likelihood of reporting bias. Is it biologically plausible that a prenatal exposure might be causally related both to spontaneous abortions and congenital malformations? This is precisely what one would expect if higher doses of the agent were embryolethal and lower doses teratogenic (12). This mixture of untoward negative reproductive outcomes has been noted in connection with the fetal alcohol syndrome. In this instance, a wide range of outcomes from increased spontaneous abortions to diverse malformations have occurred (12). The finding that no single diagnostic category accounts for the excess might be the result of exposure to multiple agents over the span of fetal growth during which different organ systems are developing.

What evidence would be most persuasive of a causal relationship between an environmental exposure and negative reproductive outcomes? Ideally, one would look find the following:

1) An increase in one or more specific adverse reproductive outcomes;

2) Data from animal studies demonstrating reproductive effects at doses comparable with those to which the study population is exposed;

3) A dose-response relationship between the exposure and the outcome, e.g., increased response at higher dose levels;

4) Geographic and temporal clustering consistent with the timing and distribution of the exposure under study;

5) Adequate control of known confounders and biases;

6) Replication of the observed association in other epidemiologic studies.

On the other extreme, a properly conducted and analyzed study which was negative and had sufficient statistical power to rule out a reasonable increase in adverse reproductive outcomes would provide persuasive evidence for the absence of an association.

The present study falls between these two extremes. In terms of the stated objectives of the study the conclusions are as follows:

1) The cluster of cardiac defect cases which had been reported represents an increase in rates in the study area which exceeds what would be expected in the basis of rates on the remainder of the county or from reports in the scientific literature. The increase appears to be limited to 1981. The distribution of cases suggests that this increase was also seen in adjacent census tracts served by other water companies.

2) Maternal risk factors for congenital heart defects are few. The factors that were examined do not explain the observed increase in rates.

3) The observed increase in rates cannot be attributed to any identified environmental factor nor, in particular, to the December 1981 leak at the Fairchild plant.

This investigation has not identified an environmental factor responsible for the increased rates of cardiac defects. In particular the time and geographic pattern of cases makes the contamination in Well #13 an unlikely explanation.

Table 1

Census Tracts Served by Great Oaks Water Company

Census Tract	Percentage of Births in Households Served by GOWC
5120.02	96%
5120.07	94%
5120.09	100%
5120.10	100%
5120.11	100%
5120.12	100%
5120.13	100%

PREGNANCY OUTCOMES IN RELATION TO WATER CONTAMINATION, 1980 - 1981
SAN JOSE, CALIFORNIA

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3 Selected Items From Questionnaire to Pregnant Women in the Los Paseos and Control Census Tracts.................

Table 2

Sources for Case Ascertainment

Source	Number of Records Reviewed	Percentage (%)
University of California San Francisco	38	4.9
Alexian Brothers	22	2.8
Los Gatos Community	13	1.7
El Camino	53	6.8
Good Samaritan	115	14.7
Kaiser Santa Clara	107	13.7
O'Connor	22	2.8
San Jose Hospital	59	7.6
Santa Clara Valley Hospital	196	25.1
St. Theresa	30	3.8
Stanford	100	12.8
Wheeler	18	2.3
Santa Clara County California Children's Service	8	1.0
	781*	100%

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*This total is larger than the number of children whose records were reviewed because of multiple records for major cases.

Table 3

Classification of Children Whose Records were Reviewed

Category	Number of Cases
Major Heart Defect	130
Other Diagnostic Categories	240
Diagnosis Uncertain	3
No Heart Defect	117
Born out of County	69
Born outside Study Period	83
Total	642

Table 4

Cases used in Data Analysis

	1981	1982A	Total
Major Cardiac Cases	71	37	108
GOWC*	10	2	12
Santa Clara County (excluding GOWC*)	61	35	96
Other Diagnostic Categories	130	81	211
GOWC*	6	5	11
Santa Clara County (excluding GOWC*)	124	76	200

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*Great Oaks Water Company service area

TABLE 5A

ALL DIAGNOSES IN MAJOR CASES (N = 130)

	COUNTY-WIDE		GOWC*	
DIAGNOSIS (ICD 9)	NUMBER DEFINITE(POSS/PROB)	PERCENT OF DEFINITE	NUMBER DEFINITE(POSS/PROB)	PERCENT DEFINIT
Common truncus (745.0)	6	1.8	0	0.0
Transposition of great vessels (745.1)	28 (1)	8.5	2	5.0
Teralogy of Fallot (745.2)	13 (1)	3.9	0	0.0
Single ventricle (745.3)	6	1.8	0	0.0
VSD (745.4)	53	16.1	5	12.5
ASD (745.5)	48	14.6	7	17.5
Endocardial cushion defect (745.6)				
with Down's syndrome	10 (1)	3.0	1	2.5
without Down's syndrome	8	2.4	2	5.0
Atresia/stenosis of valves				
aortic stenosis/atresia (746.3-.4)	6 (1)	1.8	0	0.0
other (746.00-.10,746.5)	28 (2)	8.5	4	10.0
Hypoplastic left heart (746.7)	7	2.1	1	2.5
Other specified anomalies (746.8)	18 (2)	5.5	3	7.5
Unspecified anomalies (746.9)	4 (1)	1.2	1	2.5
PDA (747.0)	56 (2)	17.0	4	10.0
Coarctation/other anomalies of aorta (747.1-.2)	21	6.4	4	10.0
Anomalies of pulmonary arteries (747.3)	7	2.1	3	7.5
Anomalies of great veins (747.4)				
Total Anomalous Venous Return (747.41)	5	1.5	1	2.5
Other	6 (1)	1.8	2	5.0
Total	330 (12)	100.0	40	100.0

---

* Area served by Great Oaks Water Company

TABLE 5B

Major Diagnoses

Each Major Case Had One or More of the Following Diagnoses

Common Truncus

Transposition of Great Vessels

Tetralogy of Fallot

Single Ventricle

Endocardial Cushion Defect

Aortic Stenosis

Tricuspid Atresia

Cor Triatriatum

Coarctation of Aorta

Idiopathic Hypertrophic Subaortic Stenosis

Tricuspid Insufficiency

Ventricular Septal Defect or Atrial Septal Defect with Congestive Heart Failure

Anomalous Pulmonary Venous Return

Hypoplastic Left Heart

Atrioventricular Block

Intrauterine PAT with Congestive Heart Failure

Dextrocardia

Valvular Stenosis

Table 6

Other Diagnostic Categories

Defect	Number of Cases
Uncomplicated VSD or ASD	103
PDA in premature with surgery and/or death	13
PDA in premature without surgery or death	44
Arrhythmia and/or functional murmur	80
Total	240

Table 7A

Major Heart Defects

1981

	Number of Cases	Number of Live Births	Cases per/1000 Live Births	Rel. Risk vs. Santa Clara Co.	Significance Probability	95% Confidence Interval
GOWC* (Includes Los Paseos)	10	1,268	7.89	2.6	(.010)	(1.3,4.9)
Los Paseos (CT5120.12)	2	132	15.15	4.9	(.066)	(1.3,18.5)
Santa Clara County (Excluding GOWC*)	61	19,628	3.11	1.0	____	____

*Area served by Great Oaks Water Company

Table 7B

Major Heart Defects (Excluding Chromosomal Defects)

1981

	Number of Cases	Number of Live Births	Cases per/1000 Live Births	Rel. Risk vs. Santa Clara Co.	Significance Probability	95% Confidence Interval
GOWC* (Includes Los Paseos)	9	1,268	7.10	2.7	(.016)	(1.4,5.5)
Los Paseos (CT5120.12)	2	132	15.15	5.9	(.041)	(1.6,22.2)
Santa Clara County (Excluding GOWC*)	51	19,628	2.60	1.0	———	———

*Area served by Great Oaks Water Company

Table 7C

Major Heart Defects
(Excluding Chromosomal Defects and/or Family History of Heart Disease)

1981

	Number of Cases	Number of Live Births	Cases per/1000 Live Births	Rel. Risk vs. Santa Clara Co.	Significance Probability	95% Confidence Interval
GOWC* (Includes Los Paseos)	8	1,268	6.31	2.7	(.016)	(1.3,5.6)
Los Paseos (CT5120.12)	2	132	15.15	6.6	(.041)	(1.7,24.7)
Santa Clara County (Excluding GOWC*)	46	19,628	2.35	1.0	___	___

*Area served by Great Oaks Water Company

Table 8A

Major Heart Defects

1981-1982A

	Number of Cases	Number of Live Births	Cases per/1000 Live Births	Rel. Risk vs. Santa Clara Co.	Significance Probability	95% Confidence Interval
GOWC* (Includes Los Paseos)	12	2,062	5.82	2.0	(.024)	(1.1,3.7)
Los Paseos (CT5120.12)	2	205	9.76	3.4	(.122)	(.9,12.6)
Santa Clara County (Excluding GOWC*)	96	33,145	2.90	1.0	——	——

*Area served by Great Oaks Water Company

Table 8B

Major Heart Defects (Excluding Chromosomal Defects)

1981-1982A

	Number of Cases	Number of Live Births	Cases per/1000 Live Births	Rel. Risk vs. Santa Clara Co.	Significance Probability	95% Confidence Interval
GOWC* (Includes Los Paseos)	11	2,062	5.34	2.2	(.019)	(1.2,4.0)
Los Paseos (CT5120.12)	2	205	9.76	4.0	(.095)	(1.1,14.8)
Santa Clara County (Excluding GOWC*)	82	33,145	2.48	1.0	____	____

*Area served by Great Oaks Water Company

Table 8C

Major Heart Defects
(Excluding Chromosomal Defects and/or Family History of Heart Disease)

1981-1982A

	Number of Cases	Number of Live Births	Cases per/1000 Live Births	Rel. Risk vs. Santa Clara Co.	Significance Probability	95% Confidence Interval
GOWC* (Includes Los Paseos)	9	2,062	4.37	2.0	(.053)	(1.0,3.9)
Los Paseos (CT5120.12)	2	205	9.76	4.4	(.080)	(1.2,16.4)
Santa Clara County (Excluding GOWC*)	74	33,145	2.23	1.0	———	———

*Area served by Great Oaks Water Company

Table 9A

Other Diagnostic Categories

1981

	Number of Cases	Number of Live Births	Cases per/1000 Live Births	Rel. Risk vs. Santa Clara Co.	Significance Probability	95% Confidence Interval
GOWC* (Includes Los Paseos)	6	1,268	4.73	.8	(.319)	(.3,1.7)
Los Paseos (CT5120.12)	0	132	.00	.0	(.434)	____
Santa Clara County (Excluding GOWC*)	124	19,628	6.32	1.0	____	____

*Area served by Great Oaks Water Company

Table 9B

Other Diagnostic Categories

1981-1982A

	Number of Cases	Number of Live Births	Cases per/1000 Live Births	Rel. Risk vs. Santa Clara Co.	Significance Probability	95% Confidence Interval
GOWC* (Includes Los Paseos)	11	2,062	5.34	.9	(.416)	(.5,1.6)
Los Paseos (CT5120.12)	0	205	.00	.0	(.290)	____
Santa Clara County (Excluding GOWC*)	200	33,145	6.03	1.0	____	____

*Area served by Great Oaks Water Company

Table 10

Distribution of Birth Month and Year for Major Cases in GOWC*

	1981		1982	
	Major Cases	Other Diagnostic Categories	Major Cases	Other Diagnostic Categories
January	1	1	0	2
February	1	0	0	1
March	1	0	0	0
April	1	0	2	0
May	1	1	0	1
June	2	0	0	0
July	0	1	0	1
August	1	1	0	0
September	1	0	0	0
October	0	1	0	0
November	1	1	0	1
December	0	0	0	1

---

*Area served by Great Oaks Water Company.

FIGURE 1
LOCATION OF THE SERVICE AREA OF THE GREAT OAKS WATER COMPANY WITHIN THE SAN FRANCISCO BAY AREA

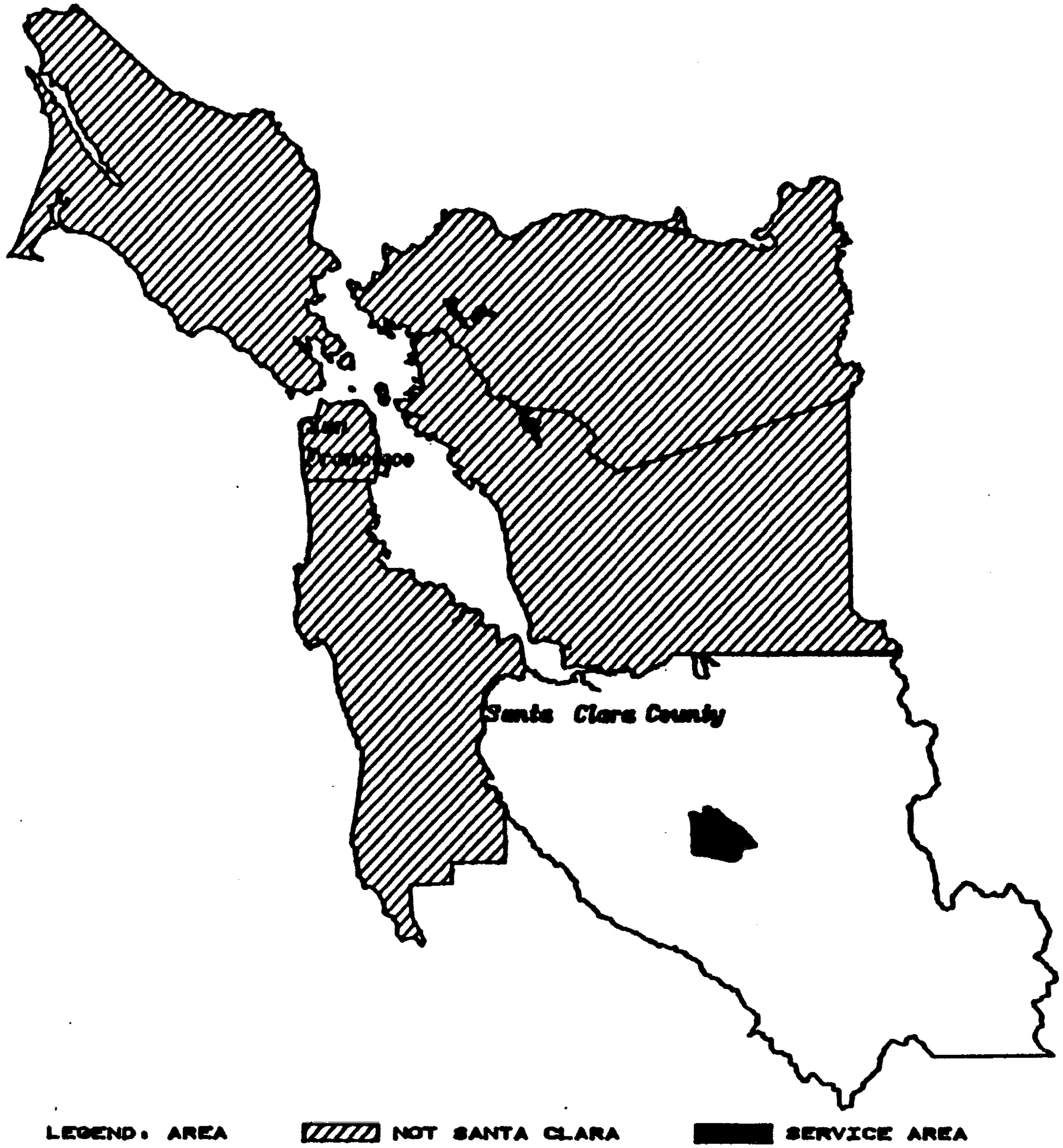
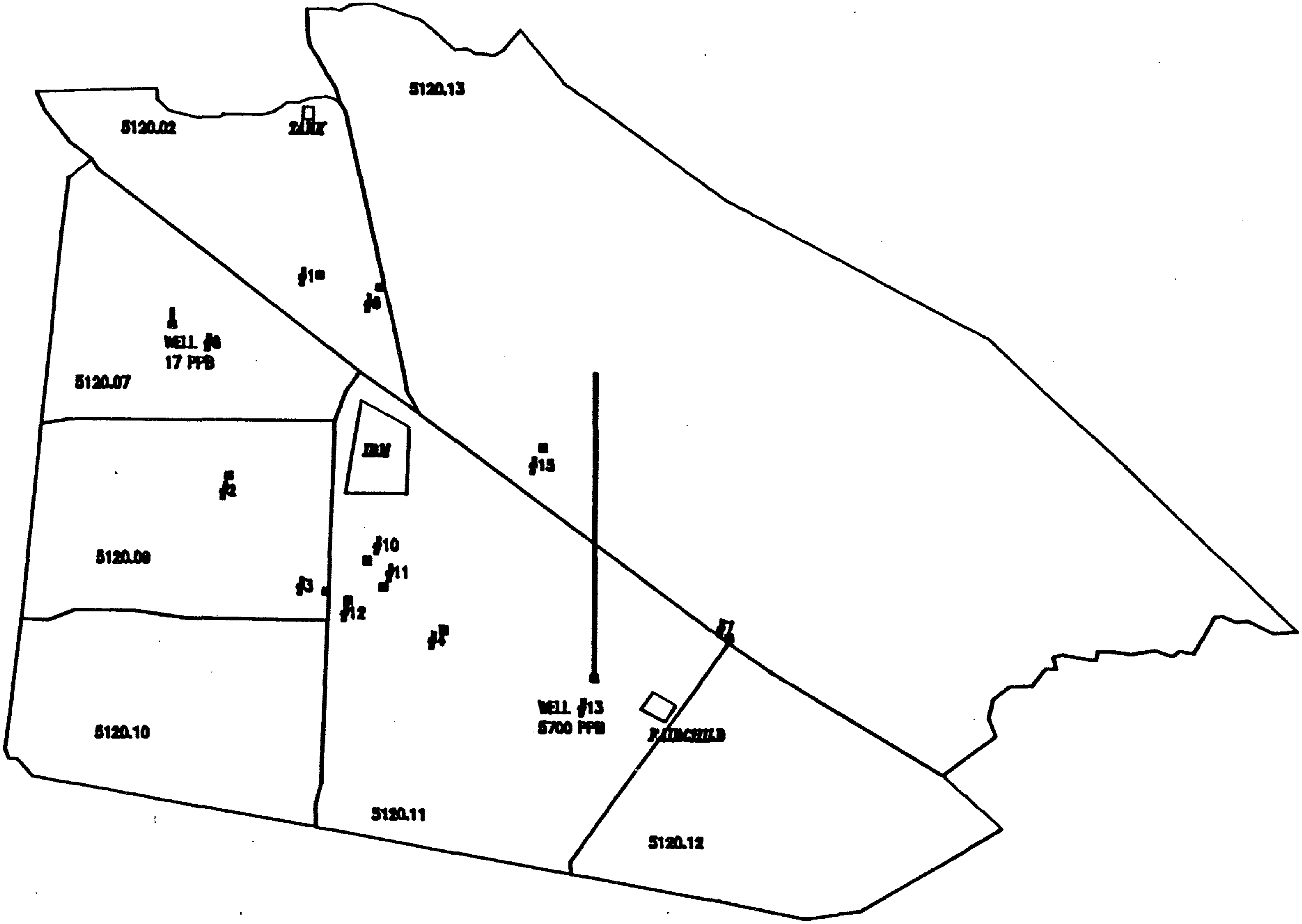
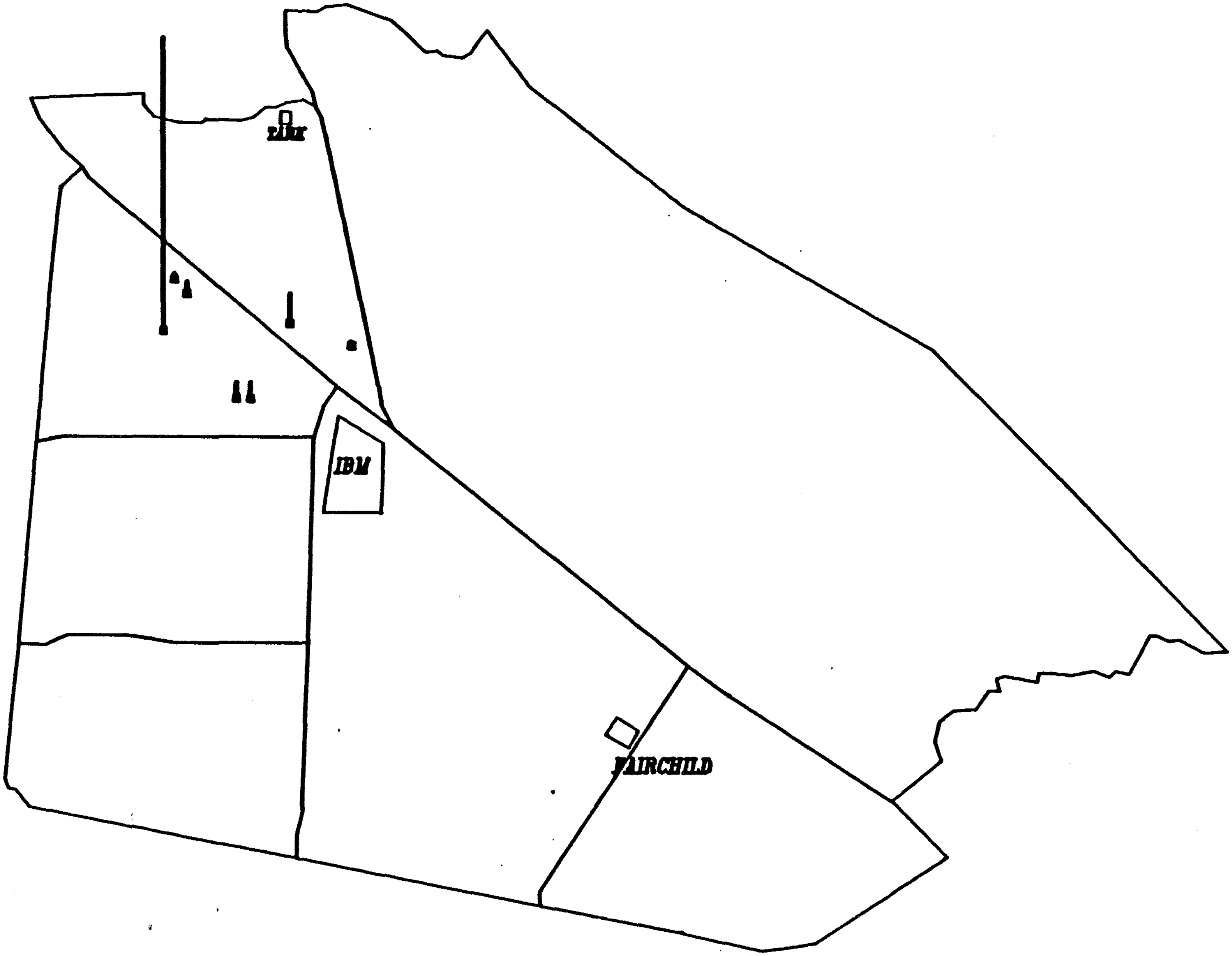


FIGURE 2
1,1,1-TRICHLOROETHANE LEVELS IN GREAT OAKS WATER COMPANY



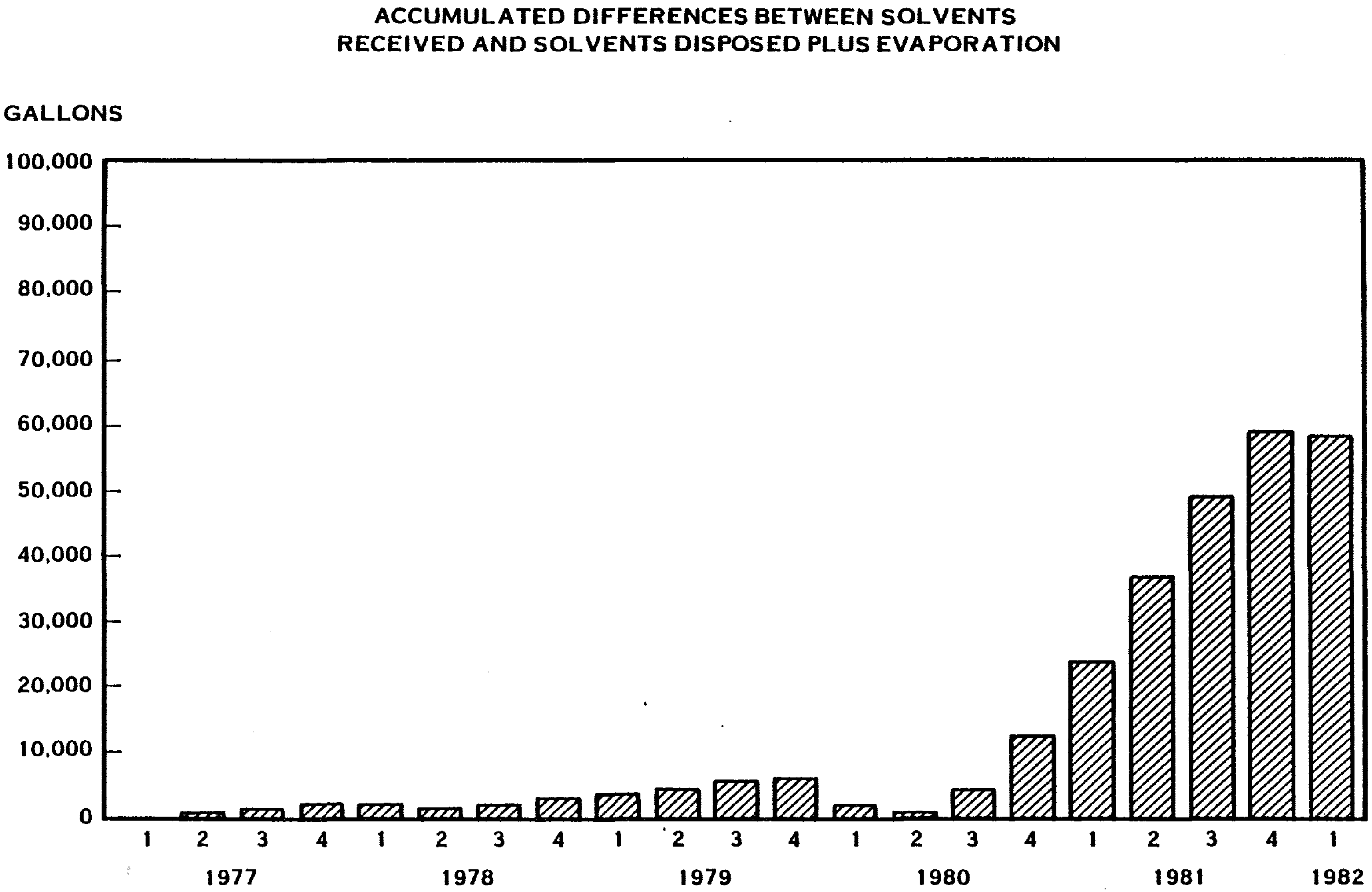
ALL GOWC WELLS (SOLID SQUARES) EXCEPT #8 AND #13 CONTAINED LESS THAN .5 PPB * (12/11/81)

FIGURE 3
1,1,1-TRICHLOROETHANE LEVELS IN PRIVATE WELLS IN THE GREAT OAKS WATER COMPANY AREA



HEIGHT OF PEAK INDICATES TCA LEVEL IN WELL---TCA VALUES RANGE FROM 2 TO 150 PPB

FIGURE 4



Source: Materials Balance Report, Fairchild Camera and Instrument Company, 1982.

FIGURE 5A

CONGENITAL HEART DISEASE in SANTA CLARA COUNTY
(January 1981 - December 1982)

LEAVE BLANK

NAME of CHILD: ____________________ __ __ __ __
LAST First Middle

SEX: ________ __

FACILITY REPORTING: ____________________ __ __

FACILITY of BIRTH (If Known): ____________________ __ __

TRANSFERRED FROM (If Applicable) FACILITY: ____________

TRANSFERRED TO (If Applicable) FACILITY: ____________

DATE of BIRTH: ____________________ __ __ __ __ __ __

GESTATIONAL AGE: Weeks <38 ___ Weeks 38-42 ___ Weeks >42 ___ UNK___ __ __ __ __ __ __

BIRTHWEIGHT: <2500g___ 2500-4000g___ >4000g___ UNK ___ __

ADDRESS: ____________________ __ __ __ __ __ __

____

____

THIS ADDRESS: At BIRTH___ At DIAGNOSIS___ UNKNOWN___ __

For CCS Only:

List names of all hospitals treating child:

____

____

____

==

EXCLUDED:

Out of County ___

No Heart Defect ___

PDA In Premature Infant ___

Older Than One Year At Initial Diagnosis___

VSD/ASD Without CHF ___

	Dx <1 yr	Dx by	CONFIRMATION						ICD CODE	PREC.
(Any) DIAGNOSIS (Include Precision)			Surg	Cath	Echo	EKG	Xray	Autpsy		
1.										
2.										
3.										
4.										
5.										
6.										

Known family history of cardiac defects:

Specify relationship:

Maternal diabetes (if stated)

Maternal thrombophlebitis (if stated)

If child died

Cause:

Date:

ABSTRACTOR:

Date:

FIGURE 5B

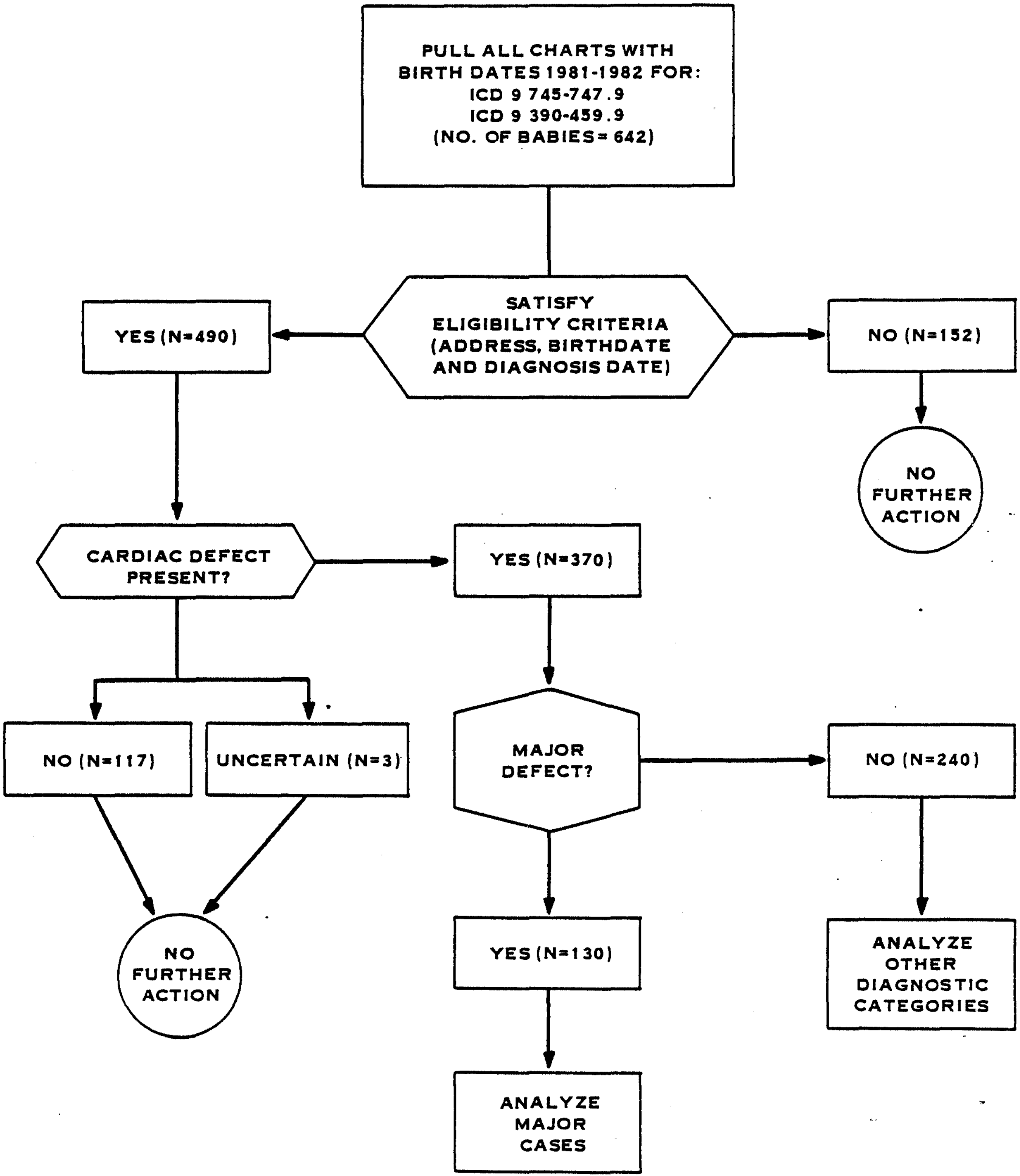


FIGURE 6 CARDIAC DEFECT STUDY
OUTLINE OF STUDY DESIGN

FIGURE 7
LOCATION OF MAJOR CARDIAC CASES IN HOMES SERVED BY GREAT OAKS WATER COMPANY: 1981

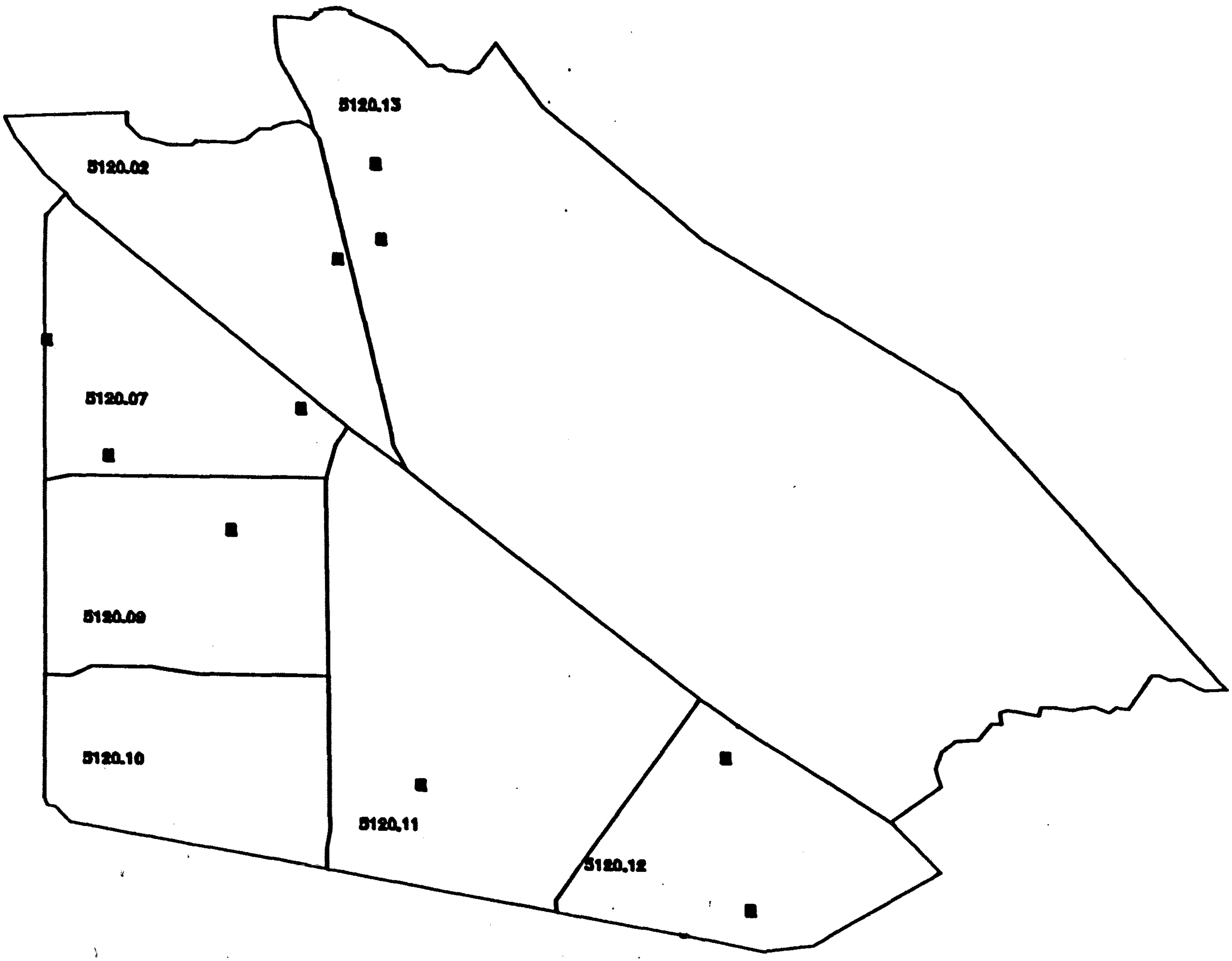
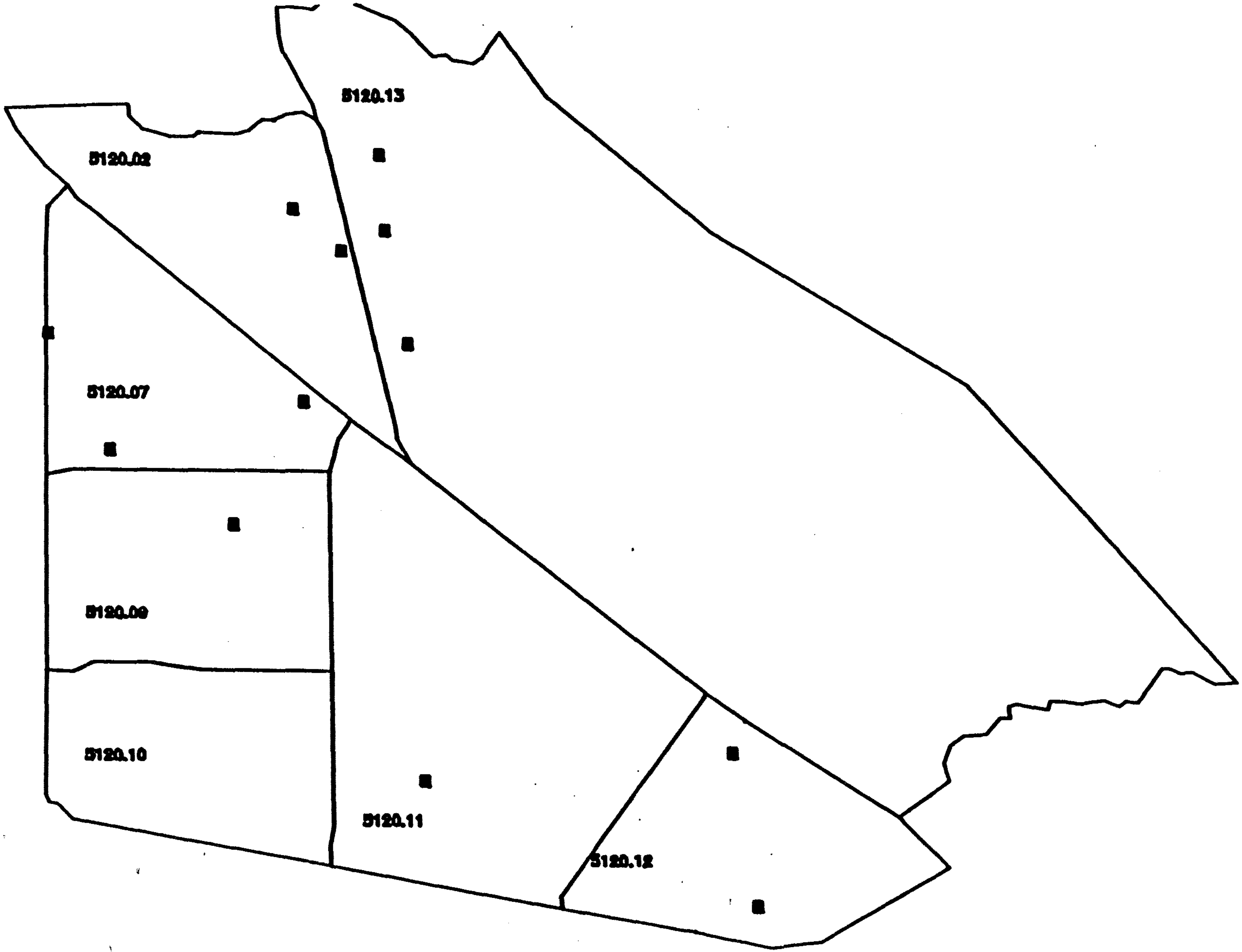


FIGURE 8
LOCATION OF MAJOR CARDIAC CASES IN HOMES SERVED BY GREAT OAKS WATER COMPANY: 1981-82A



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APPENDIX A

BIRTH STATISTICS COMPARISON: GREAT OAKS WATER DISTRICT SERVICE AREA AND SANTA CLARA COUNTY, CA, 1970-1980

PREPARED BY THE SANTA CLARA COUNTY HEALTH DEPARTMENT

Birth Defect Study

prepared for presentation to a
Community Meeting
of
Los Paseos Homeowners Asssociation

February 10, 1982

prepared by Santa Clara County Health Department

Data Sources		Indicator Used
Birth Certificate	-	Low birth weight
	-	Mention of congenital malformations*
Death Certificate	-	Neonatal death (under 28 days of age)
	-	Infant death (under 1 year of age)
Fetal Death Certificate	-	Product of conception advanced to 20 weeks gestation born with no evidence of life

*Congenital malformations: known to be under-reported. Assume quality of reporting remains constant over time and space.

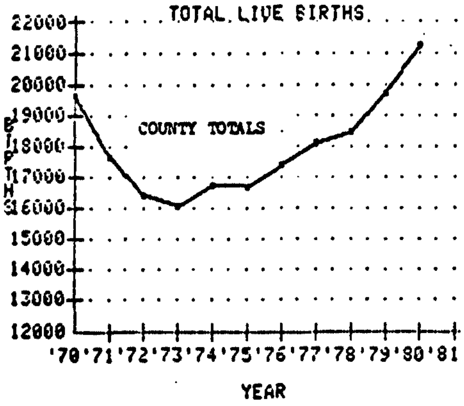
- Used as indicator - not actual count of events

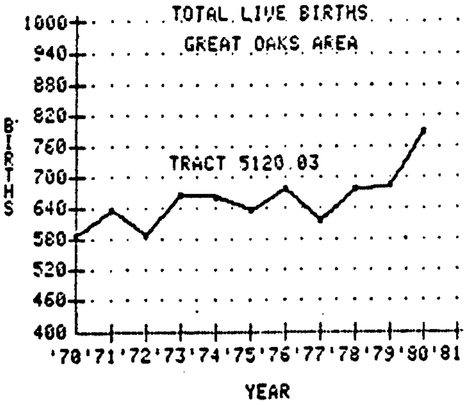
Geographic area covered

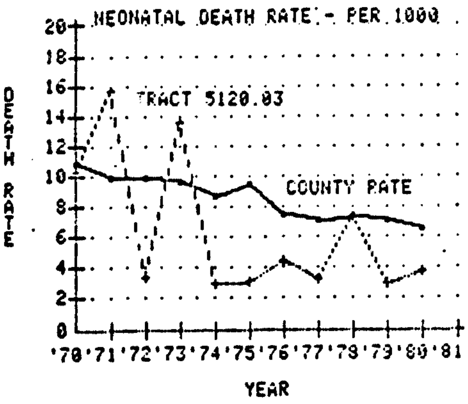
1970 - 1979	1980 - 1981
Total County & CT 120.03	120.09 120.10 120.11 120.12 120.13

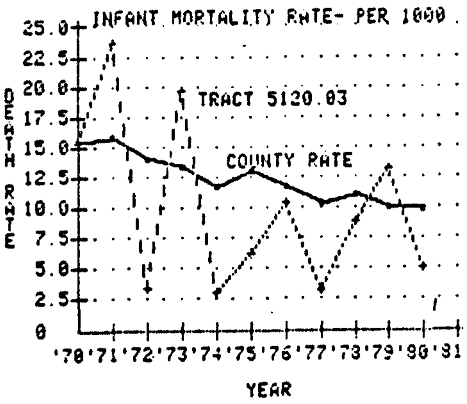
BIRTH STATISTICS COMPARISON

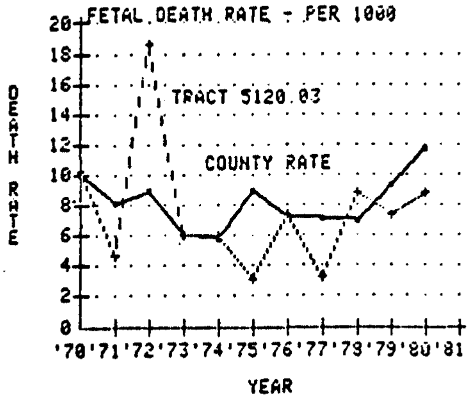
Great Oaks Water District Service Area
(Census Tract 5120.03)
&
Santa Clara County, California
1970 thru 1980











FOOTNOTES:

1. Census Tract 5120.03 is roughly equilivent to the area served by Great Oaks Water District. In 1980 this tract was split into five smaller tracts.
2. All Death rates here are measured in rates per 1000 live births.
3. Neonatal Deaths are babies born alive who die within 28 days of birth.
4. Infant Mortality (death) includes babies born alive who die within one year.
5. Fetal Deaths are babies born dead (Stillborn, who are at least 20 weeks developed.

Births, Neonatal Deaths, Infant Deaths
Total County and CT 120.03

Year		Total County				CT 120.03			
		Births	Neonatal Death	Infant Death	Fetal Death	Births	Neonatal Death	Infant Death	Fetal Death
1980	No.	21,245	140	209	248	789	3	4	7
	rate		6.59	9.84	11.67		3.80	5.07	8.87
1979	No.	19,721	140	196	183	684	2	9	5
	rate		7.09	9.94	9.28		2.92	13.16	7.31
1978	No.	18,488	135	202	129	678	5	6	6
	rate		7.30	10.93	6.98		7.37	8.85	8.85
1977	No.	18,140	129	189	128	615	2	2	2
	rate		7.11	10.42	7.06		3.25	3.25	3.25

Numbers of births increasing

Neonatal and infant death rates are generally decreasing

CT 120.03 is similar to total county: greater fluctuation due to smaller size

Graphs present a better picture

Birth Rate
Total County, CT 120.03 and CT 120.09 - 120.13

Area	Population 1980	Births - 1980		Births - 1981	
		No	Rate	No	Rate
Total County	1,295,071	21,245	16.40	21,619	16.69
CT 120.03	40,795	789	19.34*	755	18.51*
120.09	11,583	179	15.45	192	16.58
120.10	8,259	128	15.50	126	13.61
120.11	9,756	166	17.02	135	13.84*
120.12	6,474	151	23.32*	132	20.39*
120.13	4,723	165	34.94*	170	35.99*

The birth rate in the greater area CT 120.03 is significantly higher than the county average, particularly in CT's 120.11, 120.12, 120.13. This indicates a higher density of young children.

Congenital Malformations
(reported on birth certificates)
1979 - 1981

		1979	1980	1981
Total County	births	19,721	21,245	21,619
	malform	169	141	138
	rate	8.57	6.64	6.38
CT 120.03	birth	684	789	755
	malform	7	8	4
	rate	10.29	10.14	5.30
CT 120.09	birth	153	179	192
	malform	1	1	0
	rate	6.54	5.59	0.00
CT 120.10	birth	117	128	126
	malform	3	4	0
	rate	25.64	31.25	0.00
CT 120.11	birth	153	166	135
	malform	2	0	1
	rate	13.07	0.00	7.41
CT 120.12	birth	144	151	132
	malform	1	3	2
	rate	6.94	19.87	15.15
CT 120.13	birth	100	165	170
	malform	0	0	1
	rate	0.00	0.00	5.88

The number of reported congenital malformations, as well as the rate per 1,000 births, varies markedly; these variations can occur by chance alone. There is no significant difference in the observed rates.

Summary

The usual indicators of reproductive problems

- higher incidence of low birthweight babies
- increased neonatal and infant mortality rate: increased fetal death ratio
- increased reported congenital malformations

were examined, comparing CT 120.12 and CT 120.03 to the total county's experience

Found:

- significantly lower proportion of low birth weight babies
- no difference in neonatal or infant mortality, or fetal death ratio
- significantly higher birth rate
- no significant difference in reported congenital malformations

Low Birth Weight Babies

1979 - 1981

(low birth weight = ≤ 2500 gm or 5 1/2 lbs)

		1979	1980	1981
Total County	births	19,721	21,245	21,619
	low b.w.	1,083	1,276	1,200
	%	5.49	6.01	5.55
CT 120.03	birth	684	789	755
	low b.w.	37	38	24
	%	5.44	4.82	3.18
CT 120.09	birth	153	179	192
	low b.w.	11	13	4
	%	7.19	7.26	2.08 *
CT 120.10	birth	117	128	126
	low b.w.	9	6	4
	%	7.69	4.69	3.18
CT 120.11	birth	153	166	135
	low b.w.	5	7	3
	%	3.27	4.22	2.22 *
CT 120.12	birth	144	151	132
	low b.w.	10	4	2
	%	6.94	2.65 *	1.52 *
CT 120.13	birth	100	165	170
	low b.w.	2	8	11
	%	2.00 *	4.85	6.47

The proportion of mothers having low births weight babies is significantly lower than average in CT's 120.09, 120.11, and 120.12 in 1981.

APPENDIX B

TOXICOLOGICAL REVIEW OF 1,1,1-TRICHLOROETHANE AND 1,1-DICHLOROETHYLENE

B-1
1,1,1-Trichloroethane
Summary of Data on Teratology and Reproductive Effects Studies

Species	Route	Exposure	Results
1. Rat (Sprague-Dawley)	Inhalation	875 ppm 7 hr/day d 6-15 of gestation	No effects on body weight, food consumption, relative liver weight, average number of implantation sites per litter, litter size, fetal resorption, fetal sex ratios, fetal body body measurements, gross anomalies, soft tissue changes, skeletal anomalies, organs, tissues, cells. Significant increase in absolute liver weight compared to controls.
Mouse (Swiss Webster)	Inhalation	875 ppm 7 hr/day d 6-15 of gestation	Same findings as in rats but no effect on absolute liver weight
2. Mouse (ICR Swiss)	Oral Drinking water	0, 100, 300, or 1,000 mg/kg/day Two-generation	No effects on fluid consumption body weight, fertility, gestation, litter size, viability, lactation. Sporadic maternal mortality. No dominant lethal effect nor teratogenic effect.
3. Rat (Long-Evans)	Inhalation	Exposure to 2100 ppm: a) Before and after mating (++ group), 6 hr/day, 5 days/week for 2 weeks and then 7 days/week through day 20 of pregnancy b) Before mating (+-group), 6 hr/day, 7 days/week for 2 weeks c) during pregnancy (-+ group), 6 hr/day, 7 days/week through day 20 d) filtered air before mating and during pregnancy (-- group) Half of the animals evaluated for teratogenicity (sacrificed on d 21) and half for neurotoxicity (parturition on d 22-23 of pregnancy)	Teratology evaluation: Significantly increased weight gain during pregnancy in (-+) group. Significant depression in total fetal body weight and male fetal body weight in (-+) and (++) groups. Significant elevation in the total number of variations (delayed ossification of sternum, rudimentary ribs) and minor skeleta anomalies (reduced clavicle size, missing or unossified 13th rib, wavy ribs, missing or unossified 26th and 27th vertebrae, incomplete braincase closure) in (++) group. Significant elevation in the total number of minor visceral anomalies (hemorrhagic pericardium, small kidney, hydronephrotic kidney, enlarge renal medulla) in (++) group.

			Neurotoxicity evaluation: No effect on post-natal body weight or survival (1 to 12 mo of age). No significant differences observed in neurobehavioral tests of open-field activity (21 d of age), running wheel activity (40-110 d of age), and an amphetamine challenge test (110-120 d of age). Gross lesions observed at 12-mo autopsy were comparable in all groups
4. Chick embryo	Injection into air sac	5,25,50,000 umol/egg at 3 or 6 days of age	Dose-related decrease in survival. Not dose-related increase in % of malformed survivors
5. Mouse	Intratesticular injection	100,1000 mg/kg	Dose-related increase in tritiated thymidine pool size and decrease in testicular DNA synthesis

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1,1-Dichloroethylene
(Vinylidene Chloride)
Summary Data on Teratology and Reproductive Effect Studies

Species	Route	Exposure	Results
1a. Rat (Sample sizes of 44,30,30 in increasing (order of exposure)	Inhalation	0,20,80,160 ppm, 7 hr/day, at d 6-15 of gestation	At 80 and 160 ppm, maternal weight gain decreased during exposure period, and increased during post-exposure period; similar trends in food consumption. Increase in liver to body weight ratio at 160 ppm. No effect on outcome of pregnancy as indicated by number of implants, live fetuses, resorption rates, fetal sex ratios, fetal weight. No increase in major malformations. Wavy ribs and delayed ossification noted as feto-and embryotoxic manifestations of maternal toxicity at 80 and 160 ppm.
1b. Rat (N=26 for control and 24 for treated)	Oral (Drinking Water)	0,200 ppm (Daily doses of 40 mg/kg equivalent to a single 7-hr inhalation exposure to 120 ppm)	No effect on outcome of pregnancy. Significant increase in crown-rump length in fetuses.
1c. Rabbit (N =16,23, 18, in increasing order of exposure)	Inhalation	0,80, 160 ppm, 7 hr/day, at d 6-18 of gestation	At 160 ppm, body weight gain decreased during exposure and increased after termination of exposure. Increased liver to body weight ratio at 80 ppm. Increased resorption rate at 160 ppm correlated with maternal weight loss, suggestive of effect secondary to maternal toxicity. No major malformations.

2. Rats (Sprague-Dawley) N=10 males and 30 females in control group	Oral (Drinking Water)	0,50,100,200 ppm 3-generation	No adverse effect on reproduction or neonatal development. Decreased neonatal survival in F3A litters, but contradictory results in F3b and F3c litters.
3a. Rat (N=18 to 20 in treatment group. 60 in control group.	Inhalation	0,15,57,300,449 ppm 23 hr/day, at d 6-16 of gestation	Deaths (>25%) at 300 to 449 ppm no effect on weight gain and food consumption in all treated groups. Resorptions at 37 and 449 ppm. No gross external abnormalities. Fetotoxicity (soft tissue anomalies and skeletal ossification problems) in all groups but could not be evaluated for teratogenicity because maternal toxicity seen.
3bi. Mouse	Inhalation	0,15,30,57,144, 300ppm 23 hr/day at d 6-16 of gestation	Deaths (100%) at 144 and 300 ppm. Reduction of weight gain and food consumption at 30 ppm and above Resorptions at 30 and 57 ppm. No gross external abnormalities. Fetotoxicity (skeletal ossification problems) in all groups but could not be evaluated for teratogenicity because maternal toxicity seen.
3bii. Mouse (N =10-24)	Inhalation	41-112ppm (Varying combination of exposure levels and exposure periods)	Shortened exposure period lessened resorption but treatment related weight loss still evident. Soft tissue and skeletal anomalities seen but not statistically significant and occurred only when maternal welfare had been adversely affected by DCE exposure. Behavorial studies showed no major adverse effects.

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1,1,2-Trichloro-1,2,2-Trifluoroethane
(Freon 113)

Summary of Data on Teratology and Reproductive Effects Studies

Species	Route	Exposure	Results
1. Rat	Inhalation	0,5000,12500,25000 ppm 6 hr/day d 6-15 of gestation	At 25000 ppm, there was a reduction in maternal body weight gain, food utililization, and food consumption. Signs of hyperactivity during exposure to 25000 ppm. No macroscopic abnormalities or embryo toxicity. Increases in incidence of extra ribs at all exposure levels which were within background control range. No teratogenicity.
2. Rabbit	Inhalation	0, 2000, 20000 ppm 2 hr/day d 6-14 of gestation	Study inadequate for use in assessing the teratogenic potential of the chemical due to small number of pregnant animals and fetuses available.
3. Rabbit	Oral	0, 1, 5 g/kg/day d 8-11 of gestation.	Same as above.

REFERENCES

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3. Hazelton Laboratories, Inc. (1979). Teratology study in rabbits. Unpublished data of E.I. Dupont de Nemours and Company. MRO-1015, HLO-242 (1967). Final Report. Submitted to U.S. Environmental Protection Agency, 20 August, 1979. Cited by EPA (1983).

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APPENDIX C

PRIORITY POLLUTANT ANALYSIS

FOREMOST-MCKESSON ENVIRONMENTAL SERVICES

PRIORITY POLLUTANT ANALYSIS

Lab ID 000141
Sample ID Well #13
Date Received 4/6/82
Date Analyzed 4/8/82

	VOLATILES	ug/1
2V	acrolein	ND
3V	acrylonitrile	ND
4V	benzene	ND
6V	carbon tetrachloride	ND
7V	chlorobenzene	ND
10V	1,2-dichloroethane	ND
11V	1,1,1-trichloroethane	1900
13V	1,1-dichloroethane	ND
14V	1,1,2-trichloroethane	ND
15V	1,1,2,2-tetrachloroethane	ND
16V	chloroethane	ND
17V	bis (chloromethyl) ether	ND
19V	2-chloroethylvinyl ether	ND
23V	chloroform	ND
29V	1,1-dichloroethylene	20
30V	1,2-trans-dichloroethylene	ND
32V	1,2-dichloropropane	ND
33V	1,3-dichloropropylene	ND
38V	ethylbenzene	ND
44V	methylene chloride	ND
45V	methyl chloride	ND
46V	methyl bromide	ND
47V	bromoform	ND
48V	dichlorobromomethane	ND
49V	trichlorofluoromethane	ND
50V	dichlorodifluoromethane	ND
51V	chlorodibromomethane	ND
85V	tetrachloroethylene	ND
86V	toluene	ND
87V	trichloroethylene	ND
88V	vinyl chloride	ND

	PESTICIDES	ug/1
89P	aldrin	ND
90P	dieldrin	ND
91P	chlordane	ND
92P	4,4'-DDT	ND
93P	4,4'-DDE	ND
94P	4,4'-DDD	ND
95P	α-endosulfan	ND
96P	β-endosulfan	ND
97P	endosulfan sulfate	ND
98P	endrin	ND
99P	endrin aldehyde	ND
100P	heptachlor	ND
101P	heptachlor epoxide	ND
102P	α-BHC	ND
103P	β-BHC	ND
104P	γ-BHC	ND
105P	δ-BHC	ND
106P	PCB-1242	ND
107P	PCB-1254	ND
108P	PCB-1221	ND
109P	PCB-1232	ND
110P	PCB-1248	ND
111P	PCB-1260	ND
112P	PCB-1016	ND
113P	toxaphene	ND

ND = Not detected

FOREMOST-MCKESSON ENVIRONMENTAL SERVICES

PRIORITY POLLUTANT ANALYSIS

Lab ID 000136
Sample ID Well #13
Date Received 4/6/82
Date Analyzed 4/8/82

	ACID COMPOUNDS	ug/l
21A	2,4,6-trichlorophenol	ND
22A	p-chloro-m-cresol	ND
24A	2-chlorophenol	ND
31A	2,4-dichlorophenol	ND
34A	2,4-dimethylphenol	ND
57A	2-nitrophenol	ND
58A	4-nitrophenol	ND
59A	2,4-dinitrophenol	ND
60A	4,6-dinitro-o-cresol	ND
64A	pentachlorophenol	ND
65A	phenol	ND

	BASE/NEUTRAL COMPOUNDS	
1B	acenaphthene	ND
5B	benzidine	ND
8B	1,2,4-trichlorobenzene	ND
9B	hexachlorobenzene	ND
12B	hexachloroethane	ND
18B	bis(2-chloroethyl)ether	ND
20B	2-chloronaphthalene	ND
25B	1,2-dichlorobenzene	ND
26B	1,3-dichlorobenzene	ND
27B	1,4-dichlorobenzene	ND
28B	3-3'-dichlorobenzidine	ND
35B	2,4-dinitrotoluene	ND
36B	2,6-dinitrotoluene	ND
37B	1,2-diphenythydrazine (as azobenzene)	ND
39B	fluoranthene	ND
40B	4-chlorophenyl phenyl ether	ND

	BASE/NEUTRAL COMPOUNDS	ug/l
41B	4-bromophenyl phenyl ether	ND
42B	bis (2-chloroisopropyl) ether	ND
43B	bis (2-chloroethoxy) methane	ND
52B	hexachlorobutadiene	ND
53B	hexachlorocyclopentadiene	ND
54B	isophorone	ND
55B	Naphthalene	ND
56B	nitrobenzene	ND
61B	N-nitrosodimethylamine	ND
62B	N-nitrosodi-n-phenylamine	ND
63B	N-nitrosodi-n-propylamine	ND
66B	bis (2-ethylhexyl) phthalate	ND
67B	butyl benzyl phthalate	ND
68B	di-n-butyl phthalate	ND
69B	di-n-octyl phthalate	ND
70B	diethyl phthalate	ND
71B	dimethyl phthalate	ND
72B	benzo(a)anthracene	ND
73B	benzo(a)pyrene	ND
74B	3,4-benzofluoranthene	ND
75B	benzo(k)fluoranthene	ND
76B	chrysene	ND
77B	acenaphthylene	ND
78B	anthracene	ND
79B	benzo(ghi)perylene	ND
80B	fluorene	ND
81B	phenanthrene	ND
82B	dibenzo(a,h)anthracene	ND
83B	idenol(1,2,3-cd)pyrene	ND
84B	pyrene	ND
129B	2,3,7,8-tetrachlorodibenzo-p-dioxin	ND

APPENDIX D

CARDIAC DEFECTS IN GREAT OAKS WATER COMPANY SERVICE AREA VS. SELECTED COMPARISON CENSUS TRACT

APPENDIX D

Cardiac Defects in Great Oaks Water Company Service Area vs. Selected Comparison Census Tracts

Santa Clara County Health Department (SCCHD) staff used 1980 census data to compare the socio-economic characteristics of census tracts within the county. At the time this analysis was undertaken, SCCHD was interested in identifying those census tracts that were most similar to census tract 5120.12, the exposed census tract for the interview study. This census tract is referred to as Los Paseos. SCCHD identified 7 census tracts as being most similar to Los Paseos with respect to such variables as: total population, ethnic distribution, median housing cost and birth rate. These census tracts, shown in Figure D-1, were used in this analysis as a comparison area. None receives water from GOWC. A number of demographic variables have been summarized for this comparison area, the GOWC and the remainder of Santa Clara County. These are contained in Table D-1.

The rate of major cardiac malformations in 1981 for these seven census tracts was only 1.01 per 1000 live births. This is in contrast to a rate of 3.16 per 1000 in Santa Clara County (excluding GOWC). This difference may in part reflect the socio-economic differences between these this area and the rest of the county. However, these factors have not been shown to be related to rates of cardiac malformations.

In 1981 there were two cases of major cardiac defects in the Los Paseos area yielding a rate of 15.15/1000. Although based on only two cases, this rate was considerably higher than the rate for the seven census tract comparison area; the relative risk estimate for this comparison is 15.25 with a significance probability of 0.038.

The comparison of the entire GOWC with the seven census-tract area yields a relative risk estimate of 7.88 which is highly statistically significant (p=0.016). When chromosomal defects are excluded, the rates of major cardiac defects in the comparison area, and Los Paseos, remain unchanged while the rate in GOWC drops slightly to 7.10/1000. Therefore, the relative risk estimates and their confidence intervals are similar to those obtained for all major cases.

Finally, when cases with family history of cardiac disease are excluded as well as Down's syndrome cases, the single case in the seven census tract area drops out and the rate in the non-GOWC portions of the county drops to 2.35/1000. Results for 1981-82A are similar and are contained in Table D-2.

Table D-1

Demographic Characteristics of Santa Clara County (SCC)

1980 Census

Factor	GOWC[*]	Seven Census-Tract Comparison Area	Other SCC Tracts
Birth Rate	2.11	2.29	1.59
Median Persons/Unit	3.20	3.34	2.33
Median Age/Females	26.30	26.60	30.20
Median Housing Cost ($100)	1001.00	1037.00	1101.00
Ethnic Distribution[**]			
White	80.7	75.4	78.7
Black	4.1	5.2	3.4
Asian	6.8	10.6	7.7
Spanish origin	15.0	16.2	17.5

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[*] Great Oaks Water Company service area.

[**] Categories non-additive; Spanish origin may be White, Black or Asian.

Table D-2

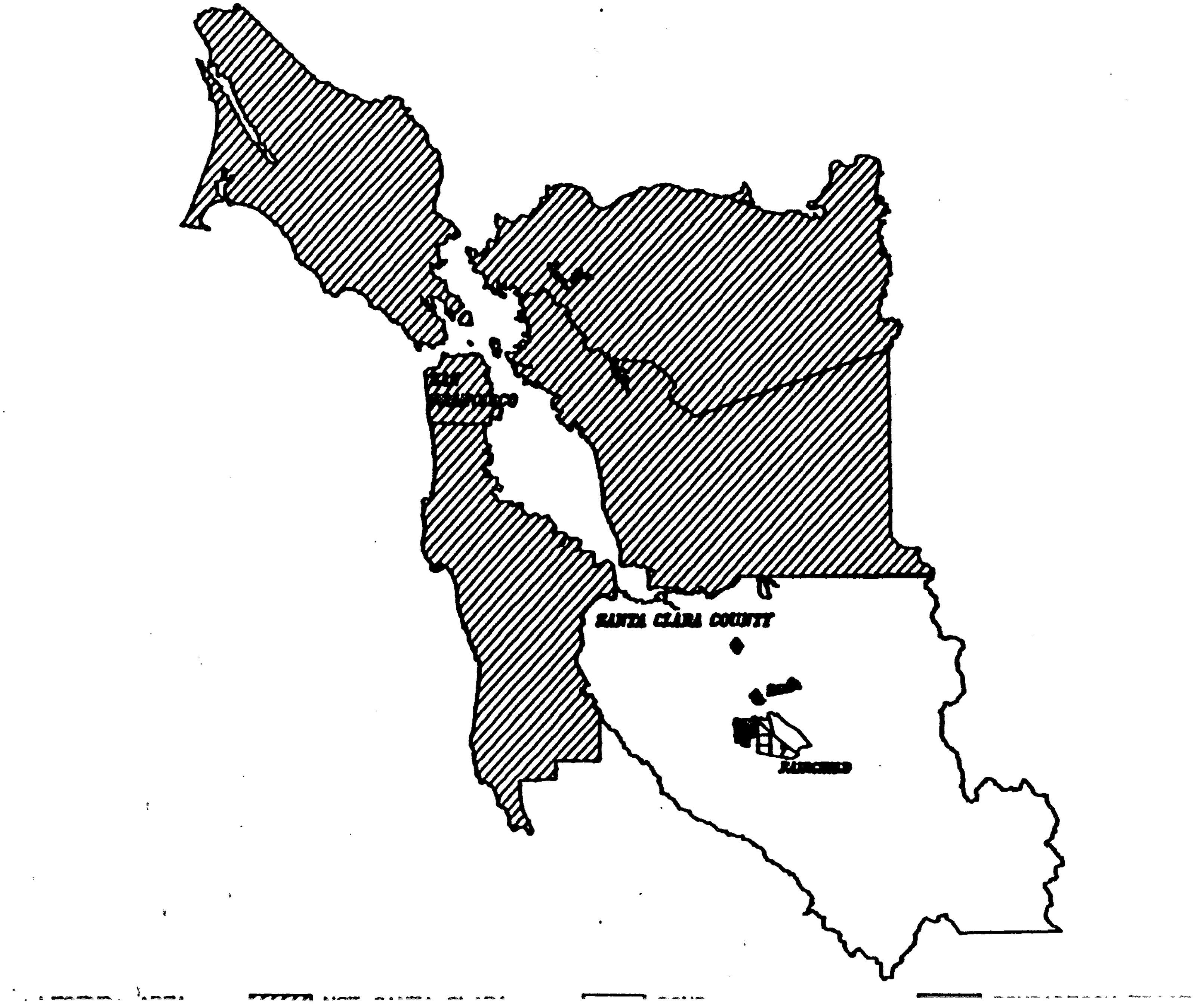
Major Heart Defects
Seven Census-Tract Comparison Area

1981

1981	Number of Cases	Number of Births	Cases per/1000 Births	Rel. Risk GOWC* vs. Seven-Tract Area	Significance Probability	95% Confidence Interval
All major cases	1	992	1.01	7.9	.016	(1.3,47.0)
Excluding Down's cases	1	992	1.01	7.1	.017	(1.2,43.3)
Excluding Down's cases and cases with family history of heart disease	0	991	0.00	.0	.010	____
1981-82A						
All major cases	3	1665	1.80	3.2	.044	(.9,9.9)
Excluding Down's cases	2	1664	1.20	4.6	.028	(1.1,18.0)
Excluding Down's cases and cases with family history of heart disease	1	1663	.60	7.3	.024	(1.2,44.6)

*Area served by Great Oaks Water Company

FIGURE D1
LOCATION OF THE GOWC AND THE SEVEN COMPARISON CENSUS TRACTS WITHIIN THE SAN FRANCISCO BAY AREA



APPENDIX E

COMPARISON OF THE DISTRIBUTIONS IN SPACE OF MAJOR CARDIAC CASES AND A RANDOM SAMPLE OF SANTA CLARA COUNTY BIRTHS

APPENDIX E

A random sample of 130 births was selected from the computer files of live births for 1981-82 to correspond in number to the 130 major cases. Birth date and address at time of birth were obtained from hard copies of the birth certificate in order to compare the spatial distribution of major cases with that of this random sample.

As can be seen in Figure E-1, four of these random births fell in GOWC in 1981. When this number is compared to the ten major cases in this area, it can be estimated that there were 2.5 as many cases in this area as would be expected. This estimate is almost exactly that of 2.55 obtained using the more traditional estimate of relative risk.

Similarly, the locations at birth of major cases and control cases born in the GOWC service area in 1981-82 are shown in Figure E-2. As can be seen, there were twice as many cases as controls in this area. Thus, it can be estimated by this method that there were twice as many major cardiac defects as expected when compared to the county as a whole. Again, this estimate agrees with the estimate obtained by a comparison of rates.

The distribution of major cases and control cases was also plotted for the entire Santa Clara County. This distribution for 1981-82A can be seen in Figure F-3. As can be seen by comparing the density of cases and controls, the excess of cases does not appear to be limited to the study area but is also present in the census tracts close to the study area toward the north and northwest. This suggests that the excess reported in this study may be part of an increase in a larger area.

FIGURE E1
LOCATION OF CARDIAC CASES AND A RANDOM SAMPLE OF SANTA CLARA COUNTY BIRTHS WITHIN HOMES SERVED BY THE GREAT OAKS WATER COMPANY (1981)

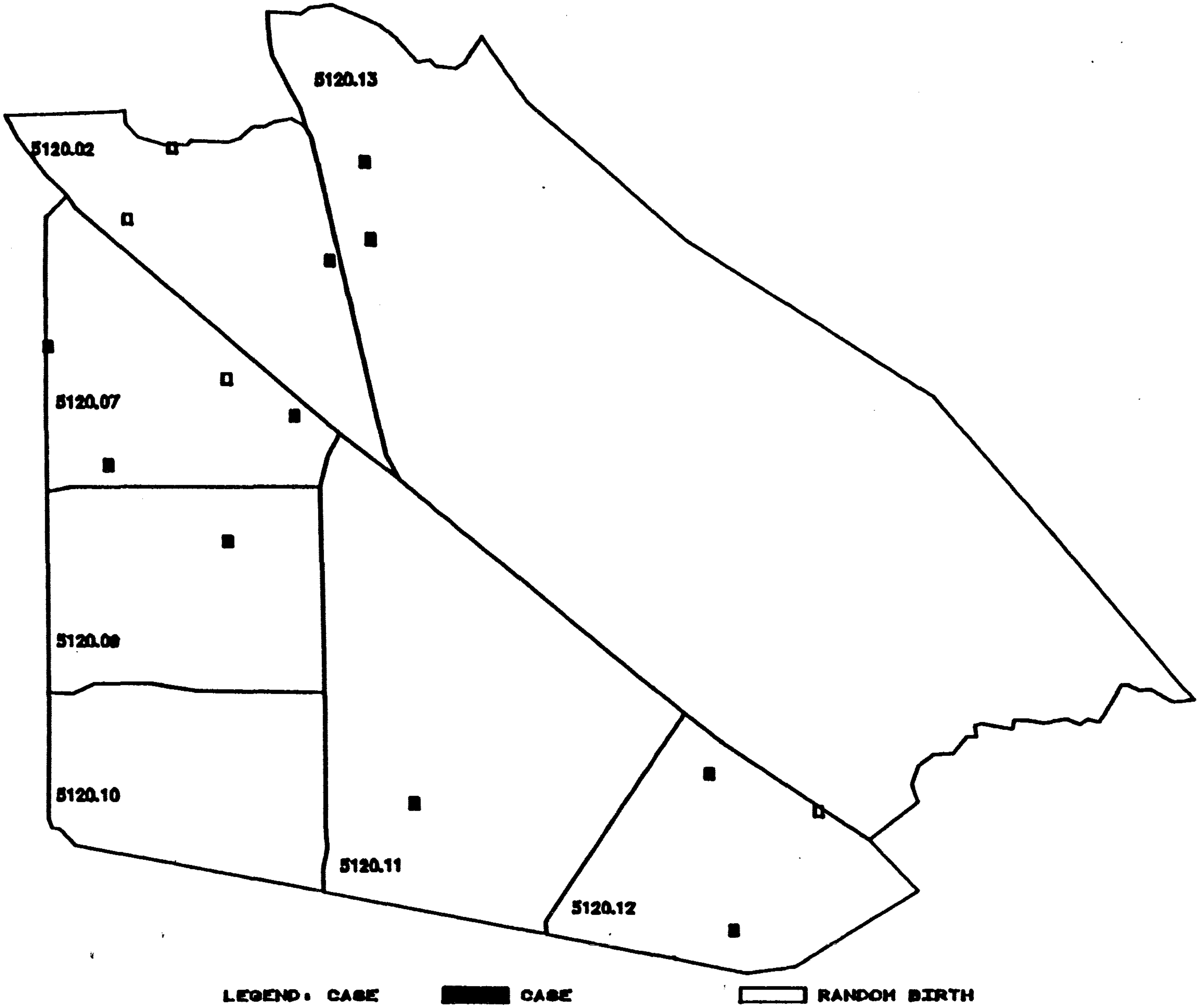


FIGURE E2
LOCATION OF CARDIAC CASES AND A RANDOM SAMPLE OF SANTA CLARA COUNTY BIRTHS
WITHIN HOMES SERVED BY THE GREAT OAKS WATER COMPANY (1981–82A)

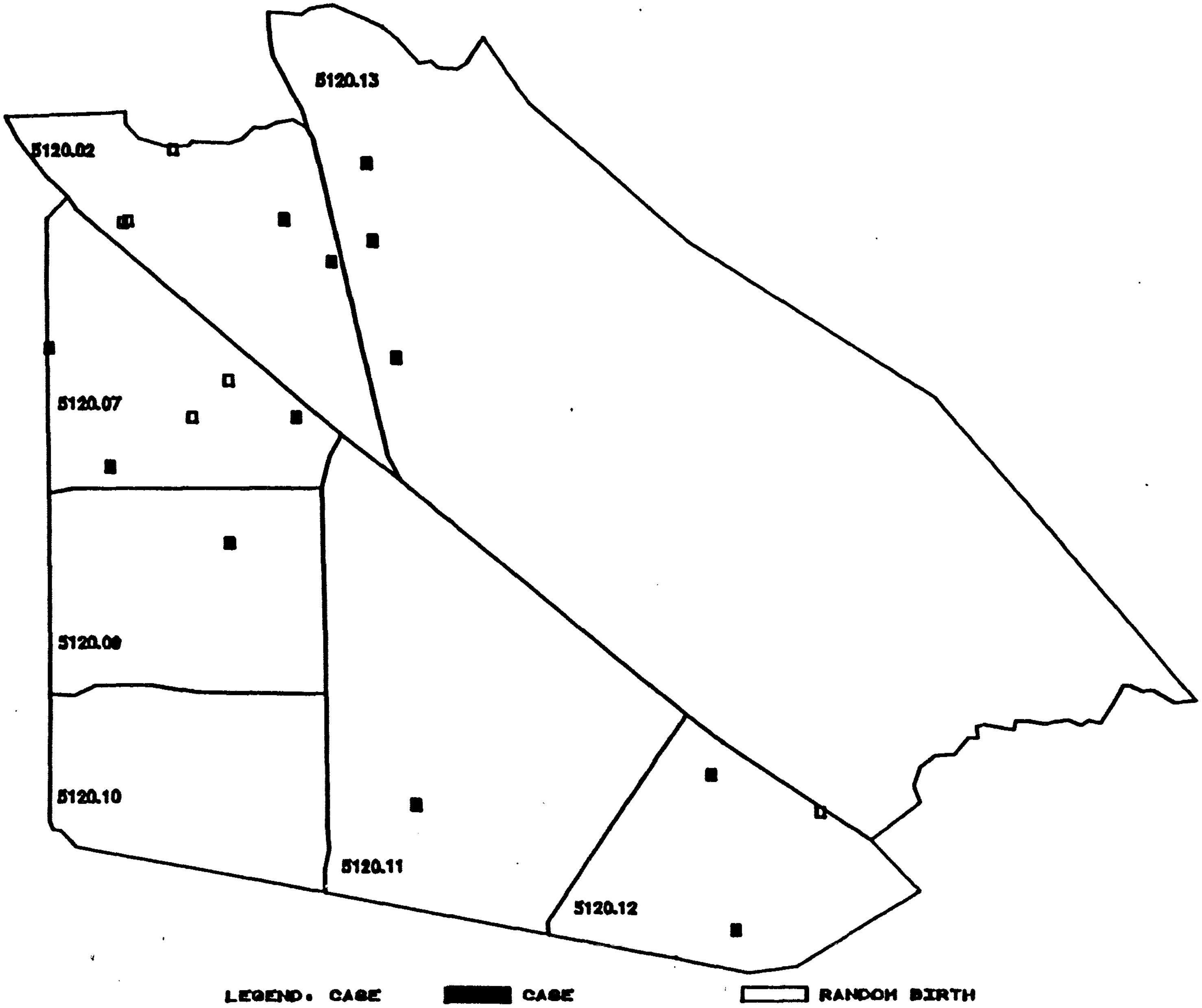
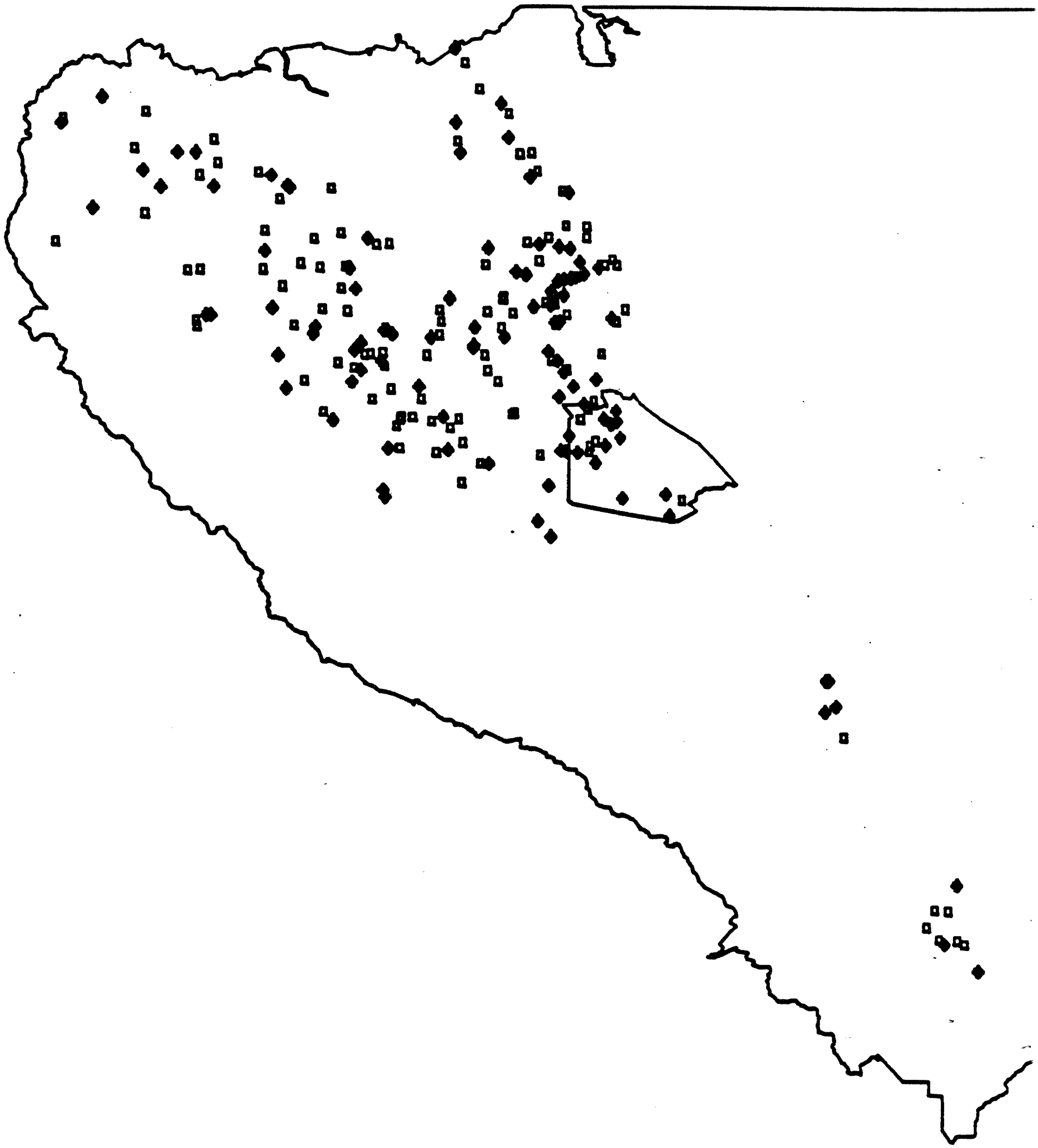


FIGURE E3
LOCATION OF CARDIAC DEFECT CASES AND RANDOM BIRTHS (1981-1982A)



CARDIAC DEFECT CASES ARE REPRESENTED BY DIAMONDS — RANDOM BIRTHS BY EMPTY SQUARES
GREAT OAKS WATER DISTRICT IS OUTLINED

APPENDIX F

SUMMARY OF WATER PRODUCTION IN GREAT OAKS WATER COMPANY BY WELL AND MONTH (1980-1981)

PREPARED BY GREAT OAKS WATER COMPANY

GREAT OAKS WATER COMPANY

Summary of Water Production (Acre Feet) - 1980

WELL	January	February	March	April	May	June	July	August	September	October	Novemmber	December
1	.910	4.200	4.820	29.370	85.606	105.150	62.850	40.890	63.580	38.830	5.180	5.900
2	45.990	45.670	83.560	133.370	99.310	82.020	72.590	71.240	145.030	133.050	113.730	62.820
3	13.270	89.990	49.090	88.970	62.400	35.760	37.760	31.930	64.270	34.490	15.470	65.750
4	67.065	95.903	168.209	143.393	175.343	174.595	177.947	178.765	167.473	168.151	64.450	55.961
7	196.204	58.377	58.305	71.139	134.154	175.574	174.625	161.413	187.120	160.544	173.879	108.794
8	3.830	8.730	5.570	29.100	1.900	91.260	144.120	190.610	44.100	5.030	4.700	9.330
9	2.490	5.040	5.830	9.010	68.290	120.750	135.890	129.960	38.630	5.050	3.590	5.510
10	21.380	22.500	22.210	16.360	42.720	83.330	40.730	22.680	29.610	13.210	15.940	32.290
11	7.180	5.610	7.540	9.460	7.370	8.210	40.750	45.460	6.130	51.630	9.110	8.810
12	10.120	11.330	27.120	13.980	21.190	30.720	54.540	91.490	13.070	8.960	72.400	68.930
13	185.230	179.610	145.880	187.700	200.770	196.510	201.340	199.070	189.680	195.570	191.740	201.480
15	4.230	.600	4.370	9.680	84.180	80.070	74.860	81.730	97.190	120.900	87.200	6.040
Total for Month	557.899	527.560	582.504	741.532	982.687	1183.949	1218.002	1245.238	1045.833	935.415	757.389	631.615

GREAT OAKS WATER COMPANY

Summary of Water Production (Acre feet) - 1981

WELL	January	February	March	April	May	June	July	August	September	October	Novemmber	December	
1	6.070	5.950	38.250	93.410	47.880	105.120	90.760	88.350	53.100	22.350	3.600	3.620	558.460
2	49.260	47.330	17.250	48.340	96.450	115.230	99.020	53.620	31.400	33.060	5.780	55.960	652.700
3	87.080	32.290	14.990	42.990	74.880	18.600	86.480	75.220	80.820	96.320	50.270	119.720	839.660
4	41.783	60.142	150.809	173.178	179.056	168.959	178.118	177.333	170.117	177.852	168.538	103.919	1749.804
7	124.870	56.837	173.631	196.695	192.369	192.744	195.100	195.391	138.027	183.495	179.257	160.475	1988.891
8	6.500	5.260	6.770	28.780	27.150	92.480	184.390	112.530	61.690	81.090	13.250	15.380	635.270
9	6.630	5.640	7.030	19.960	152.970	165.440	160.770	194.220	154.780	37.370	4.270	2.520	911.600
10	40.650	60.310	71.080	55.500	9.790	45.110	37.450	37.420	23.440	19.420	19.500	32.170	451.840
11	20.400	72.580	20.690	11.270	38.850	97.700	72.800	33.310	42.230	7.640	10.790	11.020	439.280
12	28.000	36.390	53.690	44.560	46.440	78.290	37.210	74.040	74.120	8.500	12.450	41.390	505.080
13	207.940	170.380	66.640	140.280	193.320	186.390	194.410	193.170	186.390	192.030	184.430	56.190	1971.570
15	9.780	6.240	11.760	53.630	92.350	132.160	106.530	99.660	99.390	21.760	4.570	3.180	641.010
Total for Month	628.963	559.349	632.590	908.593	1151.505	1428.223	1443.038	1334.264	1115.504	880.887	656.705	605.544	11345.165

PREGNANCY OUTCOMES IN RELATION TO WATER CONTAMINATION, 1980-1981,

SAN JOSE, CALIFORNIA

Epidemiological Studies Section
California Department of Health Services
2151 Berkeley Way
Berkeley, California 94704

January 1985

4 Response to Interview Attempt...........................

5 Pregnancy Outcome of Women at Risk.......................

6 Combined Inpatient and Outpatient Medical Record Review of a Sample of 732 Women Who Reported Not Being Pregnant in 1980 and 1981 at the Time of Household Census.....

7 Percent Distribution of Risk Factors by Census Tract.......

8 Spontaneous Abortion Rates Within Strata of Potential Confounders by Census Tract........................

9 Distribution of Illnesses, Drugs and Therapeutic X-Rays During Pregnancy....................................

10 Distribution of Occupation................................

11 Multiple Logistic Regression Coefficients for Spontaneous Abortions by Validation Method......................

12 Spontaneous Abortion Rates by Census Tract by Amount of Cold Tap Water Controlling for Anti-Nausea Pills..........

13 Month Pregnancy Identified................................

14 Spontaneous Abortion Rates by Length of Pregnancy..........

15A Congenital Anomalies Reported by Respondents with Corroboration by Either the Medical Record or the Personal Physician's Report..

15B Congenital Anomalies Reported by Respondents Where no Corroboration by a Medical Record and/or Physician Was Possible...

16 Congenital Anomalies Ascertained by Review of Medical Records Among All Respondents Who Were Residents of the Los Paseos of Control Area at the Time of Birth of Their Child and Who Were Not Interviewed............................

17 Congenital Anomalies Ascertained by Review of a Sample of 300 Medical Records of Children Whose Mothers Were Interviewed and Gave no Medical History of Congenital Malformations..................................

18 Listing of Congenital Malformations and Risk Factors Among Residents of the Study Areas........................

19 Distribution of Birthweight...............................

20 Percent of Live Births With Low Birth Weight by Year.......

21 Summary of Selected Studies of Spontaneous Abortion Incidence

Assessed by Retrospective Interviews.................

22 Spontaneous Abortion Rates by Date Pregnancy Started.......

FIGURES

1 Location of the Control and Los Paseos Census Tracts.......

2 Strategy for Selecting Study Population From Initial Enumeration.......................................

APPENDICES

A Questionnaire..

B Toxicologic Review..

PREGNANCY OUTCOMES IN RELATION TO WATER CONTAMINATION, 1980 - 1981, SAN JOSE, CALIFORNIA

ABSTRACT

On November 17, 1981 a leak of solvents from an underground storage tank was detected at the Fairchild Camera and Instrument Company in San Jose, California. Solvents were then found in Well #13 which supplied drinking water to the nearby Los Paseos community. A member of this community did an informal survey and identified a possible excess of congenital anomalies (primarily heart malformations) and spontaneous abortions. To address this concern, the California Department of Health Services carried out an epidemiologic investigation to determine: (1) whether there was an actual excess in the number of cases of spontaneous abortions and congenital anomalies, (2) whether any maternal risk factors could account for this cluster, and (3) whether this cluster was related to the leak into Well #13.

Pregnancy outcomes were assessed in two census tracts among women who conceived between January 1, 1980, and December 31, 1981. One census tract included the Los Paseos area. The other census tract, the control, had residents with similar demographic characteristics and received drinking water from another source which was found to be free of contamination when analyzed in 1982.

The Los Paseos area had a spontaneous abortion rate double that of the control area, a congenital anomaly rate triple that of the control area, and an absence of low birth-weight babies. For spontaneous abortions the odds ratio comparing the Los Paseos area with the control area, adjusting for nine possible risk factors using multiple logistic regression, was 2.4, and the 95 percent confidence interval was 1.3 to 4.2. For combined congenital malformations, the relative risk was 3.1, and the 95 percent confidence interval was 1.1 to 10.4. Assessment of the individual effects of confounding factors and recall bias suggests that no one of these could have produced this excess of spontaneous abortions and congenital malformations. There were no low birth-weight babies in the Los Paseos area while the control area had 4.9 percent (relative risk = 0, 95 percent confidence interval 0-0.5). The average birth-weights were similar for the two areas.

The actual exposures to chemical contaminants could not be determined in 1980 and 1981; therefore, the relation between the excess of spontaneous abortions and congenital anomalies, and the leak of chemicals into Well #13 is unknown.

The investigators conclude: (1) that spontaneous abortions and congenital anomalies in the Los Paseos area did occur above the expected rate; (2) that the excess cannot be attributed to differences in maternal risk factors between the two areas; and (3) that the indirect evidence about the extent and timing of exposure to contaminated water within the Los Paseos area was insufficient to determine whether the leak of chemicals into Well #13 caused the excess.

SUMMARY

INTRODUCTION

On November 17, 1981 a leak of toxic chemicals was discovered near an underground waste solvent storage tank at the Fairchild Camera and Instrument Company in San Jose, California. This tank was located about 2,000 feet from a well which supplied drinking water to the nearby Los Paseos community. On December 7, this well, Well #13 of the Great Oaks Water Company, was removed from service. Subsequently 1,1,1-trichloroethane (TCA) and 1,1-dichloroethylene (DCE) were found in the well.

Following public notification of this contamination, a member of the Los Paseos community did an informal survey and identified a possible excess of congenital anomalies (primarily heart malformations) and spontaneous abortions.

OBJECTIVES

The objectives of this study were: (1) to determine whether a cluster of spontaneous abortions and congenital malformations had actually occurred, (2) to determine whether any maternal risk factors could account for this cluster and (3) to determine whether the cluster was related to the leak into Well #13.

METHODS

The frequencies of spontaneous abortions, congenital anomalies, and low birth weight were compared in two census tracts located about four miles apart in San Jose, California. Census tract 5120.12, which will be referred to as the Los Paseos area, was selected as one of the study areas because it was the tract where the possible cluster of spontaneous abortions and congenital anomalies was identified, and it was one of two census tracts which received drinking water from Well #13. The other census tract, 5120.08, was selected as a control because its demographic characteristics were similar and it received its water from a different company whose water was apparently not contaminated.

In this study, spontaneous abortions are defined as fetal loss occurring at less than 20 weeks gestation. "Congenital anomalies" refers to a combination of "congenital malformations" (due to poor formations) and "congenital deformations" (due to mechanical constraint forces). Congenital anomalies are further restricted to codes 740-759.9 of the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM). "Low birth weight" refers to children with a weight of less than 2500 grams at birth.

To ascertain pregnancies a household enumeration was carried out in the Los Paseos and control census tracts. Women who had been pregnant any time between January 1, 1980, and December 31, 1981 were interviewed about risk factors during pregnancy, spontaneous abortions, and the presence of congenital anomalies in their children. Birth weights were obtained from birth certificates.

The study population was restricted to pregnant women who conceived between January 1, 1980, and December 31, 1981, and who lived in the study area from the first month of pregnancy until the end of pregnancy. Spontaneous abortions and congenital anomalies were validated by re-interviewing the women, by reviewing medical records, or by contacting personal physicians. To determine the degree of under-reporting of spontaneous abortions and congenital anomalies, medical records were reviewed for a large sample of women who had not reported a pregnancy during the household enumeration or had not reported a congenital anomaly during the interview.

The statistical analysis compared spontaneous abortion rates, congenital anomaly rates, and birth weights in the Los Paseos and control census tracts. In the spontaneous abortion analyses, adjustment for known risk factors was carried out using multiple logistic regression and the Mantel-Haenszel procedure.

RESULTS

The results are summarized below.

	PREGNANCY OUTCOME	Control	Los Paseos
1.	Low birth-weight rate (%) among live births at risk	4.9	0
	Mean birth weight among live births at risk	3524 gms	3521 gms
		(n=182)*	(n=145)*
2.	Spontaneous abortion rate (%) among pregnant women at risk	11.0	21.5
		(n=210)*	(n=191)*
3.	Congenital anomaly rate (%) among live births at risk	2.8	9.0
	Congenital malformation rate	2.2	6.9
	Congenital deformation rate	0.6	2.1
		(n=182)*	(n=145)*

*The numbers in parenthesis indicate the number of persons at risk

The percent of low birth-weight newborns was lower in the Los Paseos area than in the control area, (relative risk = 0, $p < 0.005$, 95 percent confidence interval 0 to 0.5) and the mean birth weights were almost the same in both study areas.

Among women at risk in 1980 and 1981, the spontaneous abortion rate assessed by interview was 21.5% in the Los Paseos area and 11.0% in the control census tract. When maternal confounding factors were considered in the multiple logistic regression, the risk of having a spontaneous abortion in the Los Paseos area, compared to the control area was 2.4 (95% confidence interval, 1.3 to 4.3, $p<0.01$). The confounding factors included were previous pregnancies; previous spontaneous abortions and stillbirths; age of mother; smoking; alcohol consumption; occupational exposures; ethnicity; and month pregnancy identified. Malathion was also considered as a possible confounder, but not was not included in the analyses because both the Los Paseos and control census tracts were sprayed with equal frequency between August and October 1981.

The overall rates of congenital malformations and congenital deformations were both three times as great in the Los Paseos area as in the control area. The rate of congenital malformations among residents of the Los Paseos area was 6.9 percent, and in the control area was 2.2 percent (relative risk = 3.1, $p = 0.04$; 95 percent confidence interval, 1.1 to 10.4).

When spontaneous abortions and congenital anomalies ascertained by interview were validated either by review of the hospital medical record, by contacting the woman's personal physician, or by re-interviewing the woman, some cases were dropped from both the Los Paseos and control areas, but the point estimates for the relative risks did not change noticeably. The excess of spontaneous abortions in the Los Paseos area did not arise from first month miscarriages, which are harder for physicians to diagnose and for women to remember. When a sample of 732 records was reviewed for women who did not report a pregnancy during the household enumeration, no cases of unreported spontaneous abortion were identified in the control area and only one unreported spontaneous abortion was identified in the Los Paseos area. One congenital malformation in the control area and two in the Los Paseos area were found during review of 287 birth records of children who were born in the study areas, but not enumerated in the household census (primarily because their families had moved before the census took place). Review of 300 birth records of children whose mothers reported no congenital anomalies during the interview showed no additional cases in the control area and one possible congenital malformation in the Los Paseos area.

The role of the leak of chemical solvents into the drinking water supply is unknown. It could not be determined when exposure started, to what degree the water was contaminated at various times in 1980 and 1981, and which contaminants were present. In the absence of specific exposure information the evidence that can be marshalled to either implicate or exonerate the leak into Well #13 is equivocal.

The substances known to have been present in Well #13, TCA and DCE, do not cause spontaneous abortions and congenital anomalies in rats, mice or rabbits but these animals are often not good models to predict human reproductive effects.

Because Well #13 was mixed with water from uncontaminated wells before reaching homes, there was dilution of the concentrations of chemical contaminants. The degree of this dilution was unknown.

The time trends of spontaneous abortions and congenital malformation rates in the Los Paseos area do not correspond to the timing of the leak according to the Fairchild Company's material balance sheet. The Fairchild material balance sheet suggests that the leak increased in the second half of 1980 and peaked sharply at the end of 1981. However, this balance sheet was constructed in 1982 after the purported cluster of spontaneous abortions and congenital malformations had been identified. It was based on company estimates of input and outflow of materials and there is uncertainty about the validity of these data.

The pattern of congenital malformations in the Los Paseos area is not one that is common for single teratogens since no specific congenital malformation was responsible for the observed overall excess. On the other hand, with the small number of cases in this study, a specific congenital malformation predominance might not be apparent. The observed pattern is consistent with more than one teratogen affecting the developing embryo at different weeks in gestation.

Congenital deformations are caused by mechanical constraint upon the developing fetus in the last trimester and are less likely to be influenced by chemicals in the environment than are malfomations. The rate of deformations as well as malformations was higher in the Los Paseos area. This implies that a teratogen may not have been responsible for either effect. The excess of congenital deformations, however, was not statistically significant and was based on small numbers.

In the companion study of heart malformations, an excess was found not only in the Los Paseos area, but also in six adjacent census tracts. Most of the people in these six adjacent tracts were unlikely to have received water from Well #13. Therefore, if one cause is sought for the findings of both studies, then contamination of Well #13 is an improbable explanation. The findings of the two studies, though, may be unrelated and may be due to different factors.

The investigators conclude: (1) that spontaneous abortions and congenital anomalies in the Los Paseos area did occur above the expected rate; (2) that the excess cannot be attributed to differences in maternal risk factors between the two areas; and (3) that the indirect evidence about the extent and timing of exposure to contaminated water within the Los Paseos area was insufficient to determine whether the leak of chemicals into Well #13 caused the excess.

INTRODUCTION

On November 17, 1981, a leak of toxic chemicals was discovered near an underground waste solvent storage tank at the Fairchild Camera and Instrument Company in San Jose, California. This tank was located about 2,000 feet from a well which supplied drinking water to nearby residential areas. On December 7, this well, Well #13 of the Great Oaks Water Company, was removed from service. Levels of TCA in Well #13 increased from 1,700 ppb on December 7 to 5,700 ppb on December 10 and reached a high of 8,800 on December 14. DCE was not measured until March 1982 and at that time was found in concentrations of 88 ppb in Well #13. Before December 1981 there were no measurements made of TCA or DCE at Well #13 or at taps in residences served by Well #13.

Following notification of this contamination, the community expressed concern about the possible health effects of this exposure. A member of the community did an informal survey and identified a possible excess of congenital anomalies, primarily heart malformations, and spontaneous abortions which occurred between December 1977 and January 1982. Most of the cases occurred among residents of census tract 5120.12 in San Jose during the years 1980 and 1981. An advisory committee was formed by the Santa Clara County Health Officer. The Epidemiological Studies Section of the California Department of Health Services (CDHS) was asked to carry out two studies. The first, a geographical study of congenital cardiac malformations in Santa Clara County is described elsewhere. The second, an interview study, focused on spontaneous abortions, congenital anomalies, and birth weight. The results of the latter study are described here.

OBJECTIVES

There were three objectives to the study:

1. To determine whether the alleged clusters of spontaneous abortions and congenital anomalies had occurred and whether there was also a cluster of low birth weight children;

2. To determine whether known maternal risk factors could account for these possible clusters;

3. To assess the relationship of these possible clusters to the leak of TCA and DCE into Well #13.

DEFINITION OF PREGNANCY OUTCOMES

Spontaneous abortions are defined as fetal loss occurring at less than 20 weeks gestation. "Congenital anomalies" refers to a combination of "congenital malformations" (due to poor formations) and "congenital deformations" (due to mechanical constraint forces). This classification was suggested by Smith[1]. Congenital anomalies are further restricted to structural defects encompassed by codes 740-759.9 of the International Classification of Disease, 9th Revision, Clinical Modification. "Low birth weight" refers to newborns with a birth weight of less than 2500 grams.

STUDY OF SPONTANEOUS ABORTIONS - METHODS

Selection of Study Areas

Census tract #5120.12, referred to as the Los Paseos area, was selected as one of the study areas for two reasons: 1) it was the tract where women expressed concern about a possible excess of congenital anomalies and spontaneous abortions; and 2) it was one of the two census tracts receiving contaminated water from Well #13.

The other study area was selected after screening all census tracts in San Jose with respect to relevant demographic variables. Census tract 5120.08 was the one most similar to the Los Paseos tract and is referred to as the control area (Table 1). The control area received its water from a different company, and no measured amounts of hazardous chemicals were found in residences served by this company in December 1982 (see Figure 1).

Data Collection

In spring 1983, the California Department of Health Services (CDHS) did an enumeration of members of each household in the Los Paseos and control areas by mail, phone, or home visit to locate women who had been pregnant in 1980 and 1981. For each household the informant was the adult who responded to the CDHS contact. The informant for the household was asked to list all household members and to state whether any pregnancies had occurred between January 1, 1980, and December 31, 1981, among women born before January 1,

1967. In the Los Paseos area, 52 percent of the informants were women; in the control area, 48 percent of the informants were women.

Altogether there were 5,291 households in the two census tracts, 2,013 in the Los Paseos area and 3,278 in the control. At least partial information was obtained from 95 percent of the households in the Los Paseos area and 94 percent of the households in the control area. Two percent of the households in each area refused to participate in the census, while an informant could not be located after repeated attempts for three percent of the households in the Los Paseos area and four percent of the households in the control area (Table 2).

Each woman reported in the enumeration to have had a pregnancy in 1980 or 1981 was sent a letter asking for her participation. Telephone interviews were then conducted to elicit information on each pregnancy and on possible confounders. The principal items covered in the questionnaire are listed in Table 3, and the complete questionnaire appears in Appendix A. The trained epidemiologic interviewers who conducted the telephone inquiries were not told whether respondents lived in the Los Paseos or control census tract.

The number of women who were pregnant at any time in 1980 and 1981 (as defined by the household enumeration) and living in the study area during the study period and at the end of pregnancy, was 250 in the Los Paseos area and 316 in the control census tract. Completed interviews were obtained for 91.2 percent of the pregnant women in the Los Paseos census tract (228 women representing 265 pregnancies) and 86.7 percent of the women in the control census tract (274 women representing 311 pregnancies). In both areas, about two percent of the women refused to be interviewed. Most of the remaining non-respondents had given a telephone number during the household enumeration which was no longer valid at the time of interview (Table 4).

Women who were pregnant in 1980-81 while living in the study areas, but who moved prior to the household enumeration in 1983, were not included in the study. The percent missed for this reason is unknown. However, it is estimated that 42 percent of pregnancies were missed in the Los Paseos area and 45 percent of pregnancies were missed in the control area, based on the number of live births (identified from birth certificates for 1980-1981) to women who were not counted in the household census.

Since exposure to water contaminants is believed to have occurred primarily in 1980 and 1981, the study population was restricted to women who conceived between January 1, 1980 and December 31, 1981 and who resided in either the Los Paseos or control area from the first month until the end of pregnancy. Figure 2 depicts the strategy employed in this study to select pregnant women at risk.

Validation of Spontaneous Abortions

Women who reported spontaneous abortions were asked to permit the CDHS to obtain medical information about their pregnancies. In cases where a woman did not consent or where it was not possible to locate the doctor or the hospital medical record, the woman was interviewed by a CDHS physician for additional information concerning spontaneous abortion(s). Four categories of spontaneous abortions were defined depending upon the validation: 1) those confirmed by the woman's personal physician; 2) those confirmed if the woman refused to release medical records but said on follow-up interview that she had a positive pregnancy test or a dilation and curettage (D & C); 3) those for which the woman's personal physician was contacted or the woman was re-interviewed, but for which there was no medical record or report of a positive pregnancy test or D & C; or 4) those for which neither the woman nor her physician could be contacted. The results of this validation are shown in Table 5.

It was important to determine the degree to which pregnancies and spontaneous abortions were under-reported in each area. About 25 percent of the women who did not report pregnancy during the household census were members of a major Northern California pre-paid health plan. Inpatient and outpatient medical records were reviewed to identify possible pregnancies in this group. The results of this validation are shown in Table 6.

Statistical Methods

The rates of spontaneous abortion in the Los Paseos and control areas were compared by the Mantel-Haenszel method across strata of each potential confounder considered. Multiple logistic regression was used to estimate odds ratios of spontaneous abortions in the Los Paseos area compared to the control area while controlling simultaneously for all confounders. The logistic analysis was carried out using all reported outcomes and was repeated using only validated outcomes.

STUDY OF SPONTANEOUS ABORTIONS - RESULTS

The spontaneous abortion rates for all self-reported pregnancies were 21.5 percent (excluding ectopic pregnancies) in the Los Paseos area, and 11.0 percent in the control area (Table 5). Within the study areas there was no apparent geographic clustering of cases. The spontaneous abortion rates based on physician confirmation were 17.3 percent in the Los Paseos area and 7.0 percent in the control area.

Nine maternal characteristics were selected as possible risk factors for spontaneous abortion. These included amount of cold tap water consumed at home during the pregnancy; number of previous pregnancies; number of previous spontaneous abortions; age of mother; amount of smoking; frequency of alcohol consumption; ethnicity; exposure of the mother to organic solvents, petrochemical products, pesticides, or x-rays during the first trimester of pregnancy; and month when the woman or her physician first identified pregnancy. A question was asked specifically about consumption of cold tap water at home to distinguish between this and consumption of bottled water or heated tap water. Heating the water drives off some volatile chemical contaminants, including TCA.

The study areas were compared with respect to these variables. The areas did not show marked differences for any of these variables, hence they would not be likely to be confounders in the analysis (Table 7). Table 8 shows that the difference in spontaneous abortion rates between the Los Paseos and control areas generally persists within each stratum of each risk factor. It is interesting to note that for the risk factor, "number of previous spontaneous abortions or stillbirths" (Table 8), the spontaneous abortion rate is greater in the Los Paseos area only for women who had no history of prior fetal loss (chi square for heterogeneity = 6.7, df=1). Mantel-Haenszel chi-squares and the associated odds ratios and confidence intervals were calculated controlling for each potential confounder separately. As seen in Table 8, all chi-squares for association of spontaneous abortions with the Los Paseos census tract area are significant at the one percent level, the point estimates for the odds ratios are all greater than 2.2, and the 95 percent confidence intervals do not include 1.

In addition, spontaneous abortion rates were calculated for the Los Paseos and control area within categories of the following variables: presence of chronic disease, acute illness in the first trimester, presence of drugs or medication in the first trimester, occupation of mother, occupation of father. Tables 9 and 10 show that within each stratum of each variable there is generally an excess of spontaneous abortions in the Los Paseos area.

A multiple logistic analysis was performed including the variables shown in Table 7. The results (Table 11) show that the excess in spontaneous abortions persists after adjustments for the other factors. The odds ratio for living in the Los Paseos area adjusting for all nine risk factors was 2.4 (95 percent confidence interval, 1.3 to 4.2). Cold tap water consumption and use of alcohol also had statistically significant regression coefficients.

The logistic analysis was repeated in two ways, first, using only spontaneous abortions that were validated either by the woman's personal physician or by follow-up interview of the mother, and second, using only those spontaneous abortions that were validated by the woman's personal physician. The results shown in Table 11 compare the logistic coefficients obtained when all reported spontaneous abortions were used with the coefficients obtained in each of the two validation groups. Little difference is seen.

The intent of the question on the amount of cold tap water consumed was to obtain a measure of the dose of TCA which the woman might have received. If the contaminated groundwater in the Los Paseos area increased the risk of spontaneous abortion, one might expect to see increasing rates of spontaneous abortions with increasing ingestion of cold tap water among those who lived in this area. In the control area one would not expect this relationship.

Drinking tap water was associated with spontaneous abortions in both of the study areas (Table 12). No spontaneous abortions occurred among those women in either area who reported drinking no cold tap water. There was an increasing rate of spontaneous abortions with increasing tap water ingestion in both the study areas.

Table 12 also shows spontaneous abortion rates in the study areas by presence or absence of anti-nausea pills during pregnancy. This stratification was done to assess whether nausea of pregnancy (which might result in less cold tap water consumption) was a confounder that explained the relationship in both study areas between cold tap water consumption and spontaneous abortions. Women who took anti-nausea medications had no spontaneous abortions. Among women not taking anti-nausea medications, spontaneous abortion rates were consistently higher at each level of cold tap water consumption in the Los Paseos area compared to the control area.

Studies such as this may be subject to recall bias, i.e., women in exposed areas may be more likely to identify and remember early pregnancies and may be more likely to interpret a late menstrual period as a symptom of spontaneous abortion than women in control areas. In this study, however, recall bias is unlikely for several reasons. First, women in both areas identified pregnancy at about the same time in gestation (Table 13). Second, the association persists when the analysis is restricted to medically validated spontaneous abortions only (Table 11). The percent of validated spontaneous abortions did not differ appreciably in the study areas (Table 5). In the control area, 65 percent of spontaneous abortions were validated by physicians while in the Los Paseos area 80 percent were similarly validated. The percent of spontaneous abortions validated either by physicians or by re-interviewing women was 91 percent in the control area and 85 percent for the Los Paseos area. In each study area there was only one spontaneous abortion for which the mother stated that she did not seek medical care of any kind (listed as "probably not miscarriages" in Table 5). We were unable to contact women or their physicians for one spontaneous abortion in the control area and five spontaneous abortions in the Los Paseos area (listed as "unable to validate" in Table 5). In the Los Paseos area these five cases are characterized as follows: two women refused permission for follow-up medical history, one woman had moved to Germany, and two women could not be located.

Third, there is no evidence of biased under-reporting in the control area compared to the Los Paseos area (Table 6). In a sample of 732 women who were enumerated in the household census and who did not report having been pregnant between January 1, 1980 and December 31, 1981, only one unreported spontaneous abortion occurred in the Los Paseos area and none were identified in the control area.

With regard to the search for unreported cases it could be argued that medical records might not show all spontaneous abortions because women with early spontaneous abortions do not seek medical care. However, if there were a biased under-ascertainment of early spontaneous abortions in the control area, the greatest excess of spontaneous abortions in the Los Paseos area should have occurred in the first month of pregnancy. Table 14 shows that this is not the case. In fact, spontaneous abortion rates are higher in the control area than in the Los Paseos area during the first month of pregnancy.

STUDY OF CONGENITAL ANOMALIES - METHODS

The method of selection of study areas and enumeration of women who had been pregnant has been described in a previous portion of this paper. The analysis of congenital anomalies was restricted to live births among women who had conceived between January 1, 1980 and December 31, 1981 and who were residents of the study area from the first month until the end of pregnancy. One hundred forty five live births in the Los Paseos census tract and 182 in the control tract qualified for the analysis (Figure 2).

For purposes of this study, the term "congenital anomalies" (ICD 740.0-759.9) refers to a combination of "congenital malformations" (due to poor formations) and "congenital deformations" (due to mechanical constraint forces). Metatarsus adductus, positional foot deformities, skin tags, nevi, mongolian spots, and undescended testicle diagnosed in the first week of life were excluded from this analysis because the diagnoses are not based on consistent criteria, with many false positives (diagnosed as abnormal, but actually normal on more thorough examination).

If a woman reported during interview that her baby was born with a congenital anomaly, confirmation of the diagnosis occurred in all cases by reviewing the medical record from the hospital of birth. One of the investigators, a pediatrician who did not know the exposure status of the women, decided whether the anomaly reported by the mother was likely to be apparent at birth or whether the diagnosis was likely to be made after birth. In the latter case confirmation by the child's personal physician was also sought.

In equivocal situations both review of the medical record and contact with the personal physician was used to validate the woman's report.

In addition, we reviewed the medical record from the birth hospital for a random sample of 300 children whose mothers were interviewed and reported no congenital anomalies. If additional malformations were found, this would give an estimate of the relation of under-reporting to census tract of residence.

If a birth certificate indicated that a child was born to parents living in either the Los Paseos or control area at the time of birth, but the parents were not enumerated at the time of census (primarily because they had changed residence), the medical record from the birth hospital was reviewed for presence or absence of congenital anomalies. There were 287 children in this group.

STUDY OF CONGENITAL ANOMALIES - RESULTS

A listing of the cases of congenital anomaly is given in Table 15. The anomalies are grouped into malformations and deformations. Malformations are more likely than deformations to be a result of teratogens. In Part A of Table 15, anomalies are listed only if they were reported by the women and confirmed either by review of the birth chart or by contacting the child's personal physician. In Part B of Table 15, confirmation had not been obtained at the time of this writing*.

Table 16 lists congenital anomalies ascertained by review of hospital birth records for children whose mother, according to the birth certificate, was a resident of either the Los Paseos or the control area at the time of birth, but not interviewed. It was unknown whether parents of these children lived in either of the study areas during any part of the first trimester of pregnancy.

Table 17 lists congenital anomalies ascertained by review of the birth records of a sample of 300 children whose mothers gave no history of congenital malformations during the interview. The mother of the single unreported case lived in the Los Paseos area during her entire pregnancy.

Congenital anomaly rates were calculated based on the report of the mother (Tables 15A and 15B). The anomalies ascertained by review of the birth record only, Table 16, were not included in rate calculations because of the uncertain residence history of the mother during pregnancy and because anomalies in this group were probably under-ascertained. The case listed in Table 17 (reported normal, but anomaly ascertained by birth hospital record) had a subarachnoid hemorrhage which was questionably attributed to an undocumented arteriovenous (AV) malformation, so this case was also not included in the rate calculations.

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*Given the specificity of the diagnosis of coloboma in Table 15B, the likelihood is that this defect will be confirmed with more intensive follow-up.

The overall rate of congenital anomalies among births to interviewees who were residents in the Los Paseos area was 9.0 percent (13/145), the malformation rate was 6.9 percent (10/145), and the deformation rate was 2.1 percent (3/145) (Table 15a, 15b). Among births to interviewees who were residents in the control area the congenital anomaly rate was 2.7 percent (5/182), the malformation rate was 2.2 percent (4/182) and the deformation rate was 0.5 percent (1/182).

The relative risk of congenital malformations in the Los Paseos area was 3.1, with a p value (Fisher's exact test) of 0.04, and a 95 percent confidence interval of 1.1 to 10.4 (Cornfield estimation for exact confidence intervals[2]). The numbers of cases are too small to control statistically for confounding factors, but a review of the malformations in Tables 15A and 15B showed no obvious risk factors which could explain the excess in the Los Paseos area (Table 18). The relative risk of congenital deformations in the Los Paseos area was 3.8, with a p value of 0.2 (Fisher's exact test) and a 95 percent confidence interval of 0.5 to 26.9.

STUDY OF LOW BIRTH WEIGHT CHILDREN - METHODS

Birth weight as reported on the birth certificate was studied for live births of women who were residents in the Los Paseos and control areas from the first month until the end of pregnancy with the estimated date of conception between January 1, 1980, and December 31, 1981 (Figure 2). The study areas were compared with respect to mean birth weight and the percent of low birth weight children.

Results

Children in the Los Paseos area had a mean birth weight of 3538 grams (standard error = 41.0) compared to 3516 grams in the control area (standard error = 43.9). The range of birth weights in the Los Paseos area was from 2608 to 5301, grams while in the control area birth weight ranged from 1290 to 5188 grams. No low birth-weight babies (less than 2500 grams) were born in the Los Paseos area, while there were nine in the control area (4.9 percent of live births). The distributions of live births by birth weight in the study areas are shown in Table 19. The p value using Fisher's exact test to compare the percent of low birth-weight children in the Los Paseos area with the percent in the control area was 0.005 (Relative risk = 0, 95 percent confidence interval, 0 to 0.5).

DISCUSSION OF ALL PREGNANCY OUTCOMES

Mean birth weights of newborns in the control and the Los Paseos areas were similar. There was a larger percent of low birth-weight babies in the control area, but the percent (4.9) is similar to the figure of 6.0 percent reported statewide in California and county-wide in Santa Clara County[3]. Table 20 shows the percent of low birth-weight babies (based on total births registered in the Los Paseos area, the control area, and county-wide for the years 1979 to 1983. The pattern in the Los Paseos and control areas do not support the hypothesis that birth weight is affected by contaminated water.

For conceptions in the two year period 1980-1981, the Los Paseos area had a spontaneous abortion rate double that of the control area and a congenital malformation rate triple that of the control area. The area difference in spontaneous abortion rates still occurred when the following possible maternal risk factors were considered in the statistical analysis: previous pregnancies; previous spontaneous abortions and stillbirths; age of mother; smoking; alcohol consumption; ethnicity; selected maternal occupational exposures; and month pregnancy was identified. When congenital malformations in the Los Paseos and control areas were examined on a case-by-case basis, known risk factors were seldom present. The risk factors examined included maternal age; family history; maternal or paternal occupational exposure to hazardous substances*; and first trimester maternal exposure to non-occupational hazardous substances*, x-rays, drugs, medications, tobacco, illness**, and alcohol. Malathion was also considered as a possible confounder but not included in the analysis because both the Los Paseos and control census tracts were sprayed with malathion bait with equal frequency between August and October 1981.

When spontaneous abortions and congenital malformations ascertained by interview were validated by review of the hospital medical record, by contacting the woman's personal physician, or by re-interviewing the women, some cases were lost from both the Los Paseos and control areas, but the point estimates for the relative risks did not change noticeably. When a sample of records was reviewed for 732 women who did not report a pregnancy at the household enumeration, no cases of spontaneous abortion were identified in the control area and only one spontaneous abortion was identified in the Los Paseos area. One congenital malformation in the control area and two cases in the Los Paseos area were found during review of 287 birth records of children who were born in the study areas but not enumerated in the household census. Also, the review of a sample of 300 birth records (50 percent of total) of children whose mothers were interviewed and gave no medical history of congenital malformations, showed no additional cases in the control area and one possible case in the Los Paseos area.

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* Defined as exposure to any of the items in question 27 of the questionnaire (see Appendix A).

** Defined as illnesses asked in questions 3, 29, 30 of the questionnaire (see Appendix A).

Rates of spontaneous abortion in the control area are similar to those reported in the literature using household interviews[6,7,8,9,10] and similar to those that the CDHS has found using comparable methodology and questionnaires (Table 21). The rate of all reported spontaneous abortions (validated or unvalidated) in the Los Paseos area (21.5 percent) is higher than the rates usually reported in the literature. The overall rate of congenital anomalies in the control area, 2.8 percent, is somewhat lower than the rate of 4 percent reported by the Centers for Disease Control in the Metropolitan Atlanta Congenital Defects Program (MACDP),[4] while the rate of 9.0 percent in the Los Paseos area is higher. However, since the method of data collection and the exclusion and inclusion criteria for anomalies in this study are different from those used by the MACDP, the congenital anomaly rates are not directly comparable.

The role of TCA and DCE in explaining these findings is unknown. It could not be determined when exposure started, to what degree Well #13 was contaminated at various times in 1980 and 1981, and which contaminants other than TCA and DCE were present. In the absence of specific exposure information the evidence that can be marshalled to either implicate or exonerate the leak into Well #13 is equivocal.

The substances known to have been present in Well #13, TCA and DCE, do not cause spontaneous abortions and congenital anomalies in rats, mice or rabbits but these animals are often not good models to predict human reproductive effects.

Because Well #13 was mixed with water from uncontaminated wells before reaching homes, there was dilution of the concentrations of chemical contaminants. However, the degree of this dilution was unknown.

The time trends of spontaneous abortion and congenital malformation rates in the Los Paseos area do not correspond to the timing of the leak according to the Fairchild company's material balance sheet (Tables 15, 22). The Fairchild material balance sheet suggests that the leak increased in the second half of 1980 and peaked sharply at the end of 1981. However, this balance sheet was constructed in 1982 after the purported cluster of spontaneous abortions and congenital malformations had been identified. It was based on company estimates of input and outflow of materials and there is uncertainty about the validity of these data.

There was an increase in spontaneous abortion rates with increasing consumption of cold tap water in both the Los Paseos and control areas. This suggests that some unrecognized confounding factor might have been present among women who abstained from drinking cold tap water. One possibility is that nausea of pregnancy (resulting in less cold tap water consumption) was such a confounder. This relates to the finding by Brandes[5] that women who experience nausea in pregnancy have a very low incidence of spontaneous abortion. There was no direct inquiry about nausea in the questionnaire, but there was a question about anti-nausea medications. The data in Table 12 are consistent with Brandes' findings; however, they are not consistent with a confounding effect of taking anti-nausea medications. Another possibility is that both areas received contaminated water but that the Los Paseos area was contaminated to a greater degree. However, this is unlikely because tests of the water in the control area in 1982 showed no chemical contamination. Thus, the relationship between the ingestion of cold tap water and spontaneous abortion in both study areas remains unexplained.

The pattern of congenital malformations in the Los Paseos area is not one that is common for single teratogens since no specific congenital malformation was responsible for the observed overall excess. On the other hand, with the small number of cases in this study, a specific congenital malformation predominance might not be apparent. The observed pattern is consistent with more than one teratogen affecting the developing embryo at different weeks in gestation.

Congenital deformations are caused by mechanical constraint upon the developing fetus in the last trimester and are less likely to be influenced by chemicals in the environment than are malfomations. The rate of deformations as well as malformations was higher in the Los Paseos area. This implies that a teratogen may not have been responsible for either effect. The excess of congenital deformations, however, was not statistically significant and was based on small numbers.

In the companion study of heart malformations, an excess was found not only in the Los Paseos area, but also in six adjacent census tracts. Most of the people in these six adjacent tracts were unlikely to have received water from Well #13. Therefore, if one cause is sought for the findings of both studies, then contamination of Well #13 is an improbable explanation. The findings of the two studies, though, may be unrelated and associated with different factors.

The investigators conclude: (1) that spontaneous abortions and congenital anomalies in the Los Paseos area did occur above the expected rate; (2) that the excess cannot be attributed to differences in maternal risk factors between the two areas; and (3) that the indirect evidence about the extent and timing of exposure to contaminated water within the Los Paseos area was insufficient to determine whether the leak of chemicals into Well #13 caused the excess.

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TABLE 1

Comparison of Los Paseos Census Tract (5120.12) and Control Census Tract (5120.08) by Selected Demographic Characteristics*

	CONTROL AREA	LOS PASEOS AREA
Median Housing Cost	$113,800	$104,600
Median Persons Per Unit	3.2	3.2
Median Age, Females	26.5	26.6
Race	100.0%	100.0%
White	84.0%	84.5%
Black	2.9%	3.6%
Asian/Pacific Islander	6.9%	6.8%
Other	6.1%	5.2%
Spanish Origin**	12.5%	11.2%
Fertility***	60.7	82.0

*Source: 1980 Census
**Persons of Spanish origin may be of any race.
***Defined as the number of live births divided by the estimated female population, age 15-44, multiplied by 1,000

TABLE 2

Response to Census of Households in Study Areas

	CONTROL AREA		LOS PASEOS AREA	
	Number	Percent	Number	Percent
Total number of households	3278	100.0	2013	100.0
Enumerated in census	3071	93.7	1920	95.4
Refused census	76	2.3	32	1.6
Vacant houses	31	0.9	21	1.0
Other non-respondent households[1]	100	3.1	40	2.0

---

[1] Unable to locate after repeated attempts.

TABLE 3

Selected Items from Questionnaire to Pregnant Women in the Los Paseos and Control Census Tracts.

Demographic:	age of mother, residential history, race and ethnicity of mother and father, occupation of mother and father, educational status of mother and father, religion of mother and father, marital status.
Pregnancy history:	number of pregnancies, outcome of each pregnancy including birth weight, stillbirth, spontaneous abortion, birth defects.
Exposure during pregnancy:	chronic illnesses, hazardous substances, x-rays, infections, drugs, alcohol, smoking, caffeine use, use of bottled water.
Family history:	consanguinity, history of birth defects.

TABLE 4

Response to Interview Attempt

	CONTROL AREA		LOS PASEOS AREA	
	Number	Percent	Number	Percent
Number of women eligible for study*	316	100.0	250	100.0
Number of women giving complete interview(s)	274	86.7	228	91.2
Refused interview	8	2.5	6	2.4
Other non-respondents**	34	10.8	16	6.4

---

*Age 15-49, pregnant any time during 1980-1981, in study area at end of pregnancy.

**Unable to locate or language problem. Most of these (24 in the control group and 12 in the Los Paseos group) represent disconnected telephone numbers and may represent women who had moved from the area before being contacted for interview.

TABLE 5

Pregnancy Outcome of Women at Risk*

	CONTROL AREA		LOS PASEOS AREA	
	Number	Percent	Number	Percent
Total number of pregnancies	210	100.0	191	100.0
Live births	182	86.7	145	75.9
Stillbirths	0	0.0	1	0.5
Spontaneous abortions	23	11.0	41	21.5
Validated by woman's doctor	(15)	(7.0)	(33)	(17.3)
Validated by woman's report of positive pregnancy test or D & C	(6)	(2.9)	(2)	(1.0)
Probably not a miscarriage	(1)	(0.5)	(1)	(0.5)
Unable to validate**	(1)	(0.5)	(5)	(2.6)
Elective abortions	5	2.4	4	2.1

*Conception between January 1, 1980 to December 31, 1981 and resident of either the Los Paseos or control area from first month of pregnancy until the end of pregnancy, excluding ectopic pregnancy.

**Women were not reachable by phone or mail or refused followup interview.

TABLE 6

Combined Inpatient and Outpatient Medical Record Review of a Sample of 732 Women Who Reported Not Being Pregnant in 1980 and 1981 at the Time of the Household Census

	CONTROL AREA		LOS PASEOS AREA	
	Number	Percent	Number	Percent
Women 15-44 who were:				
A. Enumerated, did not report being pregnant	428	100.0%	304	100.0%
B. Number of women not pregnant according to medical record review	410	95.8%	293	96.4%
C. Number of women pregnant once according to medical record review	15	3.5%	10	3.3%
D. Number of women pregnant twice according to medical record review	3	0.7%	1	0.3%
Total number of pregnancies identified by medical record review	21		12	
Live births	4		0	
Therapeutic abortions	14		9	
Spontaneous abortions (fetal loss <20 weeks)	0		1	
Stillbirth (fetal loss ≥20 weeks)	0		0	
Ectopic pregnancy	0		0	
Outcome unknown*	3		2	

*Pregnancy identified but outcome not noted on the medical record.

TABLE 7

Percent Distribution of Risk Factors by Census Tract

	CONTROL AREA		LOS PASEOS AREA	
	Number	Percent	Number	Percent
ALL PREGNANCIES	210	100.0	191	100.0
Cold tap water at home (glasses per day)				
None	26	12.4	23	12.0
1-3	85	40.5	61	31.9
4 or more	98	46.7	103	53.9
Not stated	1	0.5	4	2.1
Number of previous pregnancies				
None	50	23.8	47	24.6
1	72	34.3	65	34.0
2	44	21.0	39	20.4
3 or more	44	21.0	40	20.9
Number of previous spontaneous abortions and stillbirths				
None	152	72.4	141	73.8
1	39	18.6	35	18.3
2 or more	18	8.6	15	7.9
Not stated	1	0.5	0	0.0
Age of mother				
Less than 20	7	3.3	7	3.7
20-34	184	87.6	176	92.2
35 and over	19	9.1	8	4.2
Cigarette smoking, first trimester (packs per day)				
None	173	82.4	171	89.5
Less than half a pack	22	10.5	11	5.8
About a pack or more	15	7.1	9	4.7

TABLE 7
(continued)

	CONTROL AREA		LOS PASEOS AREA	
	Number	Percent	Number	Percent
Alcoholic beverages (frequency)				
Never	145	69.1	135	70.7
Once a month or less	42	20.0	32	16.8
At least several times a month	22	10.5	24	12.6
Not stated	1	0.5	0	--
Ethnicity				
Nonwhite	39	18.6	42	22.0
White	171	81.4	149	78.0
Occupational exposure to potentially hazardous substances (first trimester)				
Yes	10	4.8	7	3.7
No	200	95.2	184	96.3
Month pregnancy was identified				
First	74	35.2	59	30.9
Second	115	54.8	112	58.6
Third or later	21	10.0	18	9.4
Not stated	0	0.0	2	1.1

TABLE 8

Spontaneous Abortion Rates Within Strata of Potential Confounders by Census Tract

	CONTROL AREA		LOS PASEOS AREA		
	Number of Observations	Spontaneous Abortion Rate	Number of Observations	Spontaneous Abortion Rate	
ALL PREGNANCIES	210	11.0	191	21.5	
Cold tap water at home (glasses per day)					
None	26	0.0	23	0.0	Mantel-Haenszel:**
1-3	85	8.2	61	26.2	Odds ratio=2.29
4 or more	98	16.3	103	24.3	95% confidence
Not stated	1	0.0	4	0.0	interval=1.33-**3.96
					Chi-square=8.85
Number of previous pregnancies					
None	50	10.0	47	25.5	Mantel-Haenszel:**
1	72	6.9	65	23.1	Odds ratio=2.23
2	44	13.6	39	18.0	95% confidence
3 or more	44	15.9	40	17.5	interval=1.30-**3.84
					Chi-square=7.44
Number of previous spontaneous abortions or stillbirths					
None	152	7.2	141	22.7	Mantel-Haenszel:**
1	39	15.4	35	14.3	Odds ratio=2.27
2 or more	18	33.3	15	26.7	95% confidence
Not stated	1	0.0	0	--	interval=1.31-**3.91
					Chi-square=8.63

TABLE 8
(Continued)

	CONTROL AREA		LOS PASEOS AREA		
	Number of Observations	Spontaneous Abortion Rate	Number of Observations	Spontaneous Abortion Rate	
Age of mother					
Less than 20	7	14.3	7	28.6	Mantel-Haenszel:** Odds ratio=2.34 95% confidence interval=1.37-**4.10 Chi-square=9.48
20-34	184	10.3	176	19.9	
35 and over	19	15.8	8	50.0	
Cigarette smoking, first trimester (packs per day)					
None	173	9.8	171	21.6	Mantel-Haenszel:** Odds ratio=2.31 95% confidence interval=1.33-**3.99 Chi-square=8.92
Less than half a pack	22	13.6	11	36.4	
About a pack or more	15	20.0	9	0.0	
Alcoholic beverages (frequency)					
Never	145	9.0	135	17.0	Mantel-Haenszel:** Odds ratio=2.22 95% confidence interval=1.28-**3.85 Chi-square=8.06
Once a month or less	42	9.5	32	28.1	
At least several times a month	22	27.3	24	37.5	
Not stated	1	0.0	0	0.0	
Ethnicity					
Nonwhite	39	7.7	42	16.7	Mantel-Haenszel:** Odds ratio=2.28 95% confidence interval=1.32-**3.94 Chi-square=8.74
White	171	11.7	149	22.8	

TABLE 8
(Continued)

	CONTROL AREA		LOS PASEOS AREA		
	Number of Observations	Spontaneous Abortion Rate	Number of Observations	Spontaneous Abortion Rate	
Occupational exposure to potentially hazardous substances (first trimester)					
Yes	10	30.0	7	0.0	Mantel-Haenszel:** Odds ratio=2.21 95% confidence interval=1.29-**3.81 Chi-square=8.24
No	200	10.0	184	22.3	
Month mother or her doctor decided she was pregnant					
First	74	16.2	59	20.3	Mantel-Haenszel:** Odds ratio=2.28 95% confidence interval=1.31-**3.95 Chi-square=8.57
Second	115	8.7	112	25.0	
Third or later	21	4.8	18	5.6	
Not stated	0	--	2	0.0	

*Significant at the 1% level.

** Significant at the 5% level.

TABLE 9

Distribution of Illnesses, Drugs, and Therapeutic X-rays During Pregnancy

	CONTROL AREA		LOS PASEOS AREA	
	Number of Observations	Spontaneous Abortion Rate	Number of Observations	Spontaneous Abortion Rate
Total	210	11.0	191	21.5
Chronic disease ever[1]				
None reported	147	9.5	155	21.3
At least one reported	63	14.3	36	22.2
Acute illness or condition of pregnancy (first trimester)[2]				
None reported	199	10.1	186	19.9
At least one reported	11	27.3	5	80.0
Medications or other drugs (first trimester)[3]				
None reported	119	16.0	109	28.4
At least one reported	91	4.4	82	12.2
X-ray (first trimester)[4]				
None reported	199	11.1	177	22.6
At least one reported	11	9.1	14	7.1

1 Diabetes, asthma, hypertension.

2 Rubella, kidney infection, anything else with a fever of 101 degrees lasting for at least two days.

3 Anti-nausea pills, sleeping pills, diet pills, tranquilizers, estrogens, dilantin, phenobarbitol, any other prescription medication.

4 Dental, chest, pelvic or abdominal, or any other x-ray exposure.

TABLE 10

Distribution of Occupations

	CONTROL AREA		LOS PASEOS AREA	
	Number of Observations	Spontaneous Abortion Rate	Number of Observations	Spontaneous Abortion Rate
Total	210	11.0	191	21.5
Mother's Occupation[1]				
Managerial & professional specialty occupations	31	9.7	41	26.8
Technical, sales, & administrative support	73	9.6	65	24.6
Service	10	20.0	13	0.0
Operators, fabricators and laborers	13	15.4	6	0.0
No data	0	---	0	---
Did not work	83	10.8	66	21.2
Father's Occupation[2]				
Managerial & professional specialty occupations	72	9.7	88	22.7
Technical, sales, & administrative support	66	16.7	48	20.8
Service	51	5.9	34	8.8
Operators, fabricators and laborers	19	10.5	18	44.4
Not working	2	0.0	2	0.0
No data	0	0.0	1	0.0

[1] In the three months before pregnancy or during pregnancy.
[2] Usual occupation during mother's pregnancy.

TABLE 11

Multiple Logistic Regression Coefficients For Spontaneous Abortions By Validation Method

	MODEL A			MODEL B		
	Validation			Validation		
	Total Reported	Doctor or interview[1]	Doctor	Total Reported	Doctor or interview[1]	Doctor
Number of pregnancies	401	393	385	401	393	385
Number with missing data	8	8	8	4	4	4
Number in analysis	393	385	377	397	389	381
Number of spontaneous abortions	64	56	48	64	56	48
Census tract (exposed vs control)	2.35**	2.10*	2.63**	2.40**	2.13*	2.65**
95% confidence limits						
Lower	1.30	1.14	1.35	1.34	1.17	1.37
Upper	4.23	3.86	5.11	4.30	3.89	5.12
Risk factor						
Cold tap water[2]	2.13**	2.15**	1.77*	a	a	a
Previous pregnancies[2]	0.88	0.87	0.98	0.91	0.91	1.01
Previous spontaneous abortions and stillbirths[2]	1.37	1.38	1.15	1.36	1.40	1.16
Age of mother <20[3]	1.58	1.04	0.80	1.82	1.22	0.83
Age of mother >34[3]	1.89	0.93	0.72	1.81	0.94	0.72
Smoking[2]	0.97	0.99	0.76	0.94	0.94	0.71
Alcohol[2]	1.48**	1.43**	1.37*	1.46**	1.42**	1.35*
Nonwhite[3]	0.70	0.59	0.65	0.70	0.57	0.62
Occupational exposure 1st trimester[3]	1.03	0.84	0.00	1.24	1.02	0.00
Month pregnancy identified[2]	0.69	0.70	0.79	0.72	0.73	0.81

FOOTNOTES FOR TABLE 11

a Omitted from model.

1 Re-interview asked the mother whether a positive pregnancy test occurred or a D & C was performed.

2 Logistic coefficients representing the increase in relative risk for moving from one category of the variable to the next highest.

3 Odds ratios, which represent the relative risk of the presence of the confounder.

* Significant at 5% level.

** Significant at 1% level.

Notes: Odds ratios or logistic coefficients are e^b where b's are the coefficients of the equation $p = 1 / [1 + \exp - (a+b_1x_1+b_2x_2....b_nx_n)]$. p is the probability of a spontaneous abortion.

Cold tap water categories are the same as on Table 7. Previous pregnancies, previous spontaneous abortions and stillbirths, and month pregnancy identified are actual counts. Smoking and alcohol are as originally coded on the questionnaire (more detailed than in Table 7), occupational exposure is exposure to at least one of the following substances at least once a week during the first trimester of pregnancy: paint, lacquer, or varnish; organic chemicals or solvents; gasoline, kerosene, fuel oil, or other petroleum products; pesticides or herbicides; x-rays or radioactive material.

TABLE 12

Spontaneous Abortion Rates by Census Tract
by Amount of Cold Tap Water Controlling for Anti-Nausea Pills

	ANTI-NAUSEA PILLS				NO ANTI-NAUSEA PILLS			
	CONTROL AREA		LOS PASEOS AREA		CONTROL AREA		LOS PASEOS AREA	
Glasses of cold tap water/day	Number	Spontaneous Abortion Rate	Number	Spontaneous Abortion Rate	Number	Spontaneous Abortion Rate	Number	Spontaneous Abortion Rate
Total	33	0.0	13	0.0	175	13.1	176	23.3
None	4	0.0	3	0.0	22	0.0	20	0.0
One	1	0.0	0	0.0	14	7.1	16	12.5
2-3	8	0.0	1	0.0	61	9.8	44	31.8
4 or more	20	0.0	8	0.0	77	20.8	95	26.3
Unknown	0	0.0	1	0.0	1	0.0	1	0.0

NOTE: Excludes 2 pregnancies in the Los Paseos area and 2 in the control area with unknown anti-nausea pill use.

TABLE 13

Month Pregnancy Identified

	CONTROL AREA		LOS PASEOS AREA	
Month Decided Pregnant	Number of Observations	Percent	Number of Observations	Percent
Total	210	100.0	191	100.0
First	74	35.2	59	30.9
Second	115	54.8	112	58.6
Third	19	9.1	16	8.4
Fourth	1	0.5	0	0.0
Fifth	1	0.5	2	1.1
Unknown	0	0.0	2	1.1

TABLE 14

Spontaneous Abortion Rates By Length of Pregnancy

	CONTROL AREA			LOS PASEOS AREA		
	Number of Observations	Number of Spontaneous Abortions	Spontaneous Abortion Rate	Number of Observations	Number of Spontaneous Abortions	Spontaneous Abortion Rate
Length of Pregnancy						
Total						
One month	210	4	1.9	191	2	1.0
Two months	205	12	5.9	187	22	11.8
Three months	189	4	2.1	164	13	7.9
Four months	185	2	1.1	150	4	2.7
Five months	183	1	0.5	146	0	0.0

NOTE: The denominator for each time period was obtained by subtracting the number of spontaneous abortions and therapeutic abortions during the previous time period from the previous demonimator.

TABLE 15A

Congenital Anomalies Reported by Respondents With Corroboration by Either the Medical Record or the Personal Physician's Report

CONTROL AREA (n = 182)

Malformation	Month and Year of Birth
Ventricular septal defect	12/80
Hypospadius (second degree)	07/81
Tetralogy of Fallot	07/82

Deformation	Month and Year of Birth
Sternocleidomastoid torticollis	10/80

TABLE 15A
(continued)

LOS PASEOS AREA (n = 145)

Malformation	Month and Year of Birth
Nasolacrimal stenosis	09/80
Ventricular septal defect requiring surgery	09/80
Low set ears, slight micrognathia	01/81
Benign form of webbing of 4th and 5th toes	03/81
Omphalocele, right talipes equinovarus	04/81
Total anomalous pulmonary venous return	11/81
Imperforate anus, kidney anomaly not otherwise specified	12/81
Down's Syndrome	05/82
Congenital diaphragmatic hernia	06/82
Cleft lip and palate	06/82

Deformation	Month and Year of Birth
Left club foot	10/80
Internal tibial torsion	10/80
Right talipes equinovarus	02/81

TABLE 15B

Congenital Anomalies Reported by Respondents Where no Corroboration by a Medical Record and/or a Physician Was Possible.

CONTROL AREA

Malformation	Month and Year of Birth
Coloboma of right eye	07/81

Deformation	Month and Year of Birth
NONE	

LOS PASEOS AREA

Malformation	Month and Year of Birth
NONE	

Deformation	Month and Year of Birth
NONE	

TABLE 16

Congenital Anomalies Ascertained by Review of Medical Records Among All Respondents Who Were Residents of the Los Paseos or Control Area at the Time of Birth of Their Child and Who Were Not Interviewed*

CONTROL AREA (n = 168)

Malformation	Month and Year of Birth
Microcephaly, cataracts, hydroanencephly	05/81

Deformation	Month and Year of Birth
NONE	

LOS PASEOS AREA (n = 119)

Malformation	Month and Year of Birth
Hypospadius, degree not specified	05/80
Robin anomalad	09/82

Deformation	Month and Year of Birth
Club foot	02/82

---

*Reason interview not done was usually because the respondents moved out of the area.

TABLE 17

Congenital Anomalies Ascertained by Review of a Sample of 300 Medical Records of Children Whose Mothers Were Interviewed and Gave no Medical History of Congenital Malformations

CONTROL AREA (n = 165)

Malformation	Month and Year of Birth
NONE	

Deformation	Month and Year of Birth
NONE	

LOS PASEOS AREA (n = 135)

Malformation	Month and Year of Birth
Subarachnoid hemorrhage questionably secondary to an arteriovenous malformation	06/81

Deformation	Month and Year of Birth
NONE	

TABLE 18

Listing of Congenital Malformations and Risk Factors Among Residents of Study Areas

CONTROL AREA

-----------DEMOGRAPHICS	CHARACTERISTICS----------			-------------------MATERNAL	EXPOSURE HISTORY-FIRST	TRIMESTER--------------------				
Congenital Malformation	Age of Mother <20 or >35	Maternal Occupational Exposure to Hazardous Substances	Paternal Occupational Exposure to Hazardous Substances	Hazardous Substance Exposure	X-Ray	Sickness	Medications Other Than Vitamins Acetaminophen Aspirin	Cigarette Smoking	Alcohol Consumption	Family History of Congenital Malformation
Ventricular septal defect	no	no	no	no	no	no	no	no	no	paternal cousin
Second degree hypospadius	yes	no	no	no	no	no	no	no	no	no
Tetralogy of Fallot	no	no	no	no	no	no	Bendectin 2nd month	no	no	no
Coloboma	no	no	no	no	no	no	no	1/2 pack per day	no	no

TABLE 18
(continued)

LOS PASEOS AREA

-----DEMOGRAPHIC CHARACTERISTICS-----				-----MATERNAL EXPOSURE HISTORY-FIRST TRIMESTER-----						
Congenital Malformation	Age of Mother <20 or >35	Maternal Occupational Exposure to Hazardous Substances	Paternal Occupational Exposure to Hazardous Substances	Hazardous Substance Exposure	X-Ray	Sickness	Medications Other Than Vitamins Acetaminophen, Aspirin	Cigarette Smoking	Alcohol Consumption	Family History of Congenital Malformations
Nasolacrimal stenosis	no	no	no	no	no	no	no	no	no	no
Ventricular septal defect	no	no	no	no	no	no	no	no	no	no
Low set ears	no	no	no	no	no	no	no	1/2 pack per day	no	no
Webbing of toes	no	no	no	no	no	no	no	no	no	no
Omphalocele	no	no	no	no	no	no	no	no	no	no
Total anomalous pulmonary venous return	no	no	no	no	no	no	no	no	no	no
Imperforate anus, kidney anomaly NOS	no	no	no	no	no	no	no	no	no	no
Down's Syndrome	no	no	no	no	no	no	Bendectin, 3rd month	no	no	no
Congenital diaphragmatic hernia	no	no	no	no	no	no	Pepto Bismol, 2nd month	no	no	no
Cleft lip and palate	no	no	no	no	no	no	no	no	no	no

TABLE 19

Distribution of Birthweight

	CONTROL AREA		LOS PASEOS AREA	
	Number	Percent	Number	Percent
Birthweight in grams				
Total	182	100.0	145	100.0
Less than 2500	9	4.9	0	0.0
1000-1499	1	0.6	0	0.0
1500-1999	2	1.1	0	0.0
2000-2499	6	3.3	0	0.0
2500 grams or more	173	95.1	145	100.0
2500-2999	19	10.4	19	13.1
3000-3499	52	28.6	53	36.6
3500-3999	71	39.0	49	33.8
4000-4499	23	12.6	18	12.4
4500-4999	7	3.9	5	3.5
5000-5499	1	0.6	1	0.7
Range	1290 - 5188		2608 - 5301	
Mean	3516.1		3537.6	
Standard error of mean	43.9		41.0	

t = 0.36, degrees of freedom = 324.3, p = 0.72

TABLE 20

Percent of Live Births With Low Birth Weight by Year

YEAR	CONTROL AREA	LOS PASEOS AREA	SANTA CLARA COUNTY
1979	N/A	6.94	5.49
1980	3.61	2.65	5.44
1981	4.32	1.52	4.06
1982	5.26	4.50	5.72
1983	3.91	2.94	5.76

TABLE 21

Summary of Selected Studies of Spontaneous Abortion Incidence Assessed by Retrospective Interviews

Author	Group Studied	Definition of Spontaneous Abortion	Incidence of Spontaneous Abortion per 100 Pregnancies
Calif State Dept. of Health Services (unpublished 1984)	Residents living near the Purity Dumpsite Fresno County, CA, and control (interview by any adult respondent in the household)	Fetal loss any time	8.0 in exposed 9.7 in control
Calif State Dept. of Health Services (unpublished 1983)	Women living near the McColl dumpsite in Fullerton, CA, and control women	Fetal loss ≤20 weeks	8.5 in exposed 6.9 in control
Hemminki[6] et al (1982)	Women engaged in sterlizing instruments with chemical agents in hopitals, and control hospital workers	Not stated	11.3 - Exposed 10.6 - Control
Smith[7] (1982)	Wives of 2,4,5-T chemical applicators and control wives	Not stated	8.6 - Exposed 9.3 - Control (Excludes therapeutic abortions in denominator)
Himmelberger et al[8] (1978)	Women anesthesiologists, nurse anesthetists, women operating room personnel	Fetal Loss ≤20 weeks	14.0 (Excludes therapeutic abortions in denominator)

TABLE 21
(Continued)

Author	Group Studied	Definition of Spontaneous Abortion	Incidence of Spontaneous Abortion per 100 Pregnancies
Rothman[9] (1977)	Population based survey of women using oral contraceptives prior to pregnancy and women not using oral contraceptives	Not stated	11.0
Warburton, Fraser[10] (1964)	Women referred to a university hospital genetics clinic	Fetal loss <28 weeks	14.7 (Excludes therapeutic abortions in denominator)

TABLE 22

Spontaneous Abortions Rates by Date Pregnancy Started

Date Pregnancy Started	CONTROL AREA		LOS PASEOS AREA	
	Number of Observations	Spontaneous Abortion Rate	Number of Observations	Spontaneous Abortion Rate
All Time Periods	210	11.0	191	21.5
Jan-Jun, 1980	51	9.8	47	23.4
Jul-Dec, 1980	50	12.0	50	20.0
Jan-Jun, 1981	50	14.0	49	20.4
Jul-Dec, 1981	59	8.5	45	22.2

FIGURE 1

Location of the Control and Los Paseos Census Tracts

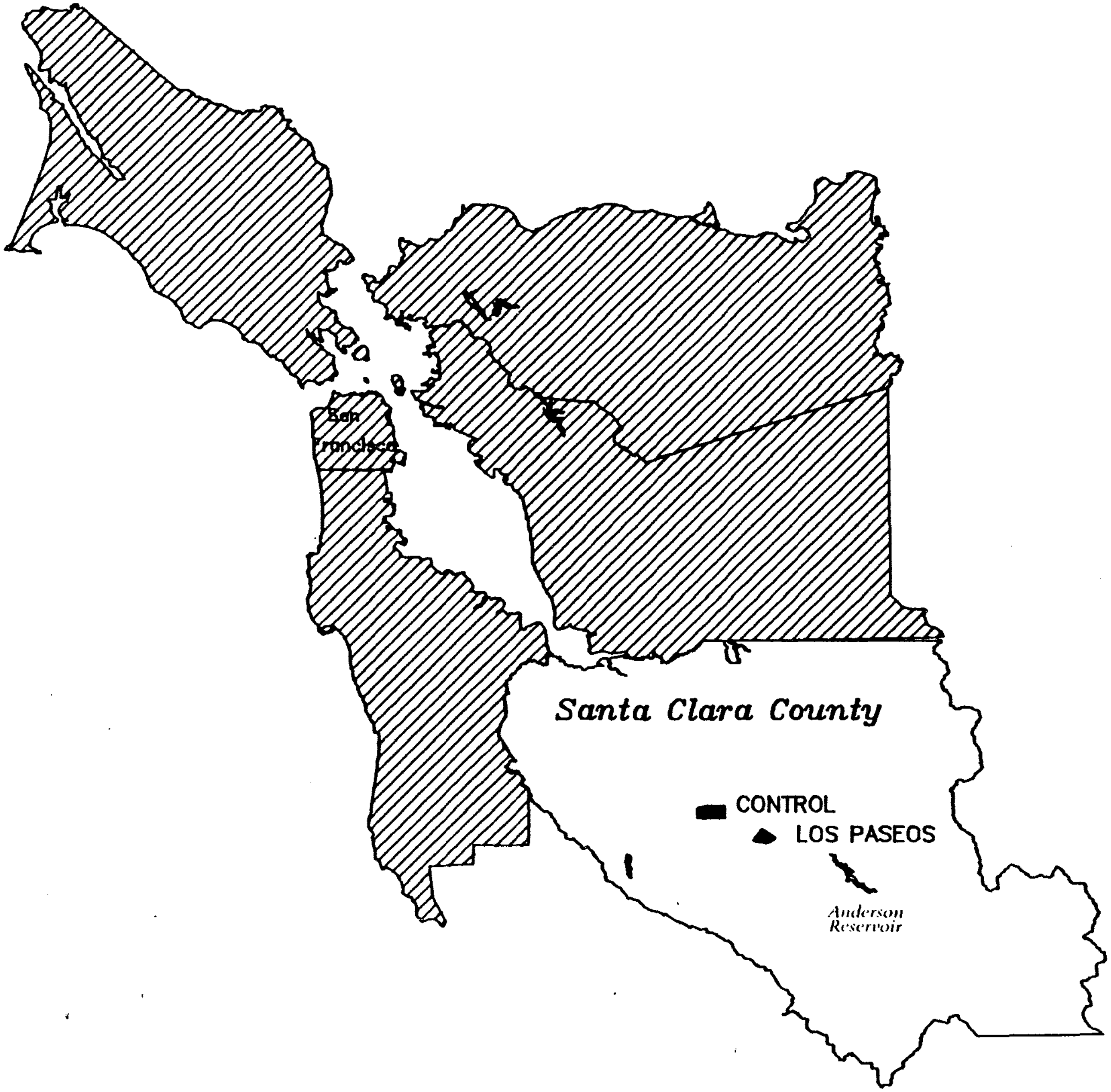
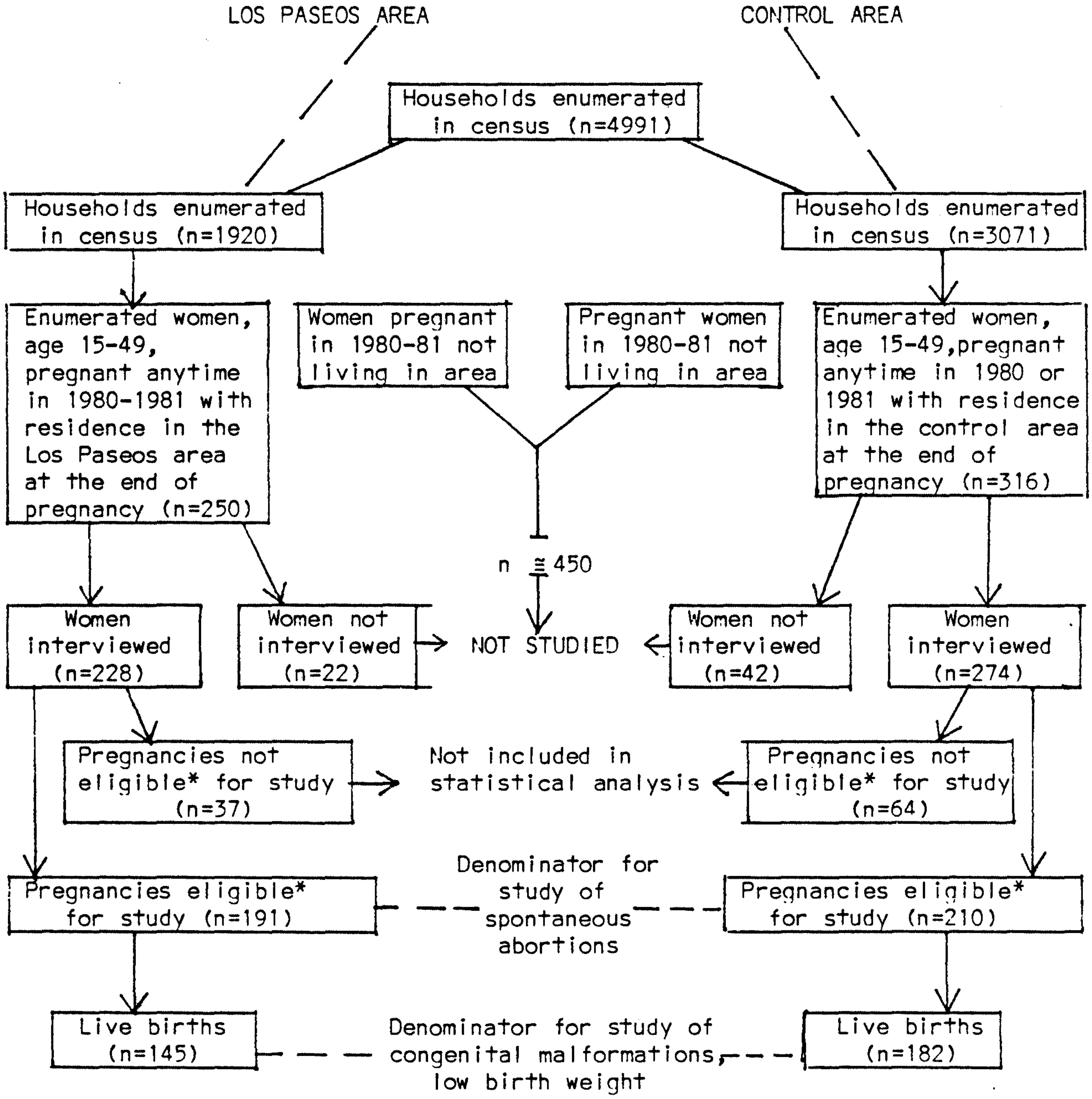


FIGURE 2

Strategy for Selecting Study Population from Initial Enumeration


LOS PASEOS AREA
CONTROL AREA
Households enumerated in census (n=4991)
Households enumerated in census (n=1920)
Households enumerated in census (n=3071)
Enumerated women, age 15-49, pregnant anytime in 1980-1981 with residence in the Los Paseos area at the end of pregnancy (n=250)
Women pregnant in 1980-81 not living in area
Pregnant women in 1980-81 not living in area
Enumerated women, age 15-49, pregnant anytime in 1980 or 1981 with residence in the control area at the end of pregnancy (n=316)
n ≅ 450
Women interviewed (n=228)
Women not interviewed (n=22)
NOT STUDIED
Women not interviewed (n=42)
Women interviewed (n=274)
Pregnancies not eligible* for study (n=37)
Not included in statistical analysis
Pregnancies not eligible* for study (n=64)
Pregnancies eligible* for study (n=191)
Denominator for study of spontaneous abortions
Pregnancies eligible* for study (n=210)
Live births (n=145)
Denominator for study of congenital malformations, low birth weight
Live births (n=182)

*Eligibility is defined as residing in the Los Paseos or Control area from the first month until the end of pregnancy (not necessarily at the same address) with the estimated date of conception between January 1, 1980 and December 31, 1981. Ectopic pregnancies are not eligible.

APPENDIX A

QUESTIONNAIRE

TIME INTERVIEW STARTED ____________ 9-12

ID ____________ 1-4

INTERVIEWER'S INITIALS ____________ 13-15

DATE ____________ 5-8

PREGNANCY OUTCOME QUESTIONNAIRE

Hello. May I speak to -----------------------. This is ------------- from the State Department of Health Services. I'm interviewing for the health study of women in San Jose who have been pregnant. Did you receive a letter from us concerning this study? PAUSE.

I'd like to interview you now if it's convenient. It probably won't take more than about 15 minutes. All information you give me is confidential and will be used only in statistical summaries. PAUSE.

IF RESPONDENT REFUSES, TRY TO FIND OUT WHY, TO ANSWER ANY OBJECTIONS AND TO PERSUADE THE RESPONDENT TO ALLOW HERSELF TO BE INTERVIEWED. THE RESPONDENT MAY CONFIRM THE LEGITIMACY OF THE STUDY BY PHONING STUDY HEADQUARTERS AT --------------AND ASKING FOR-------------. DO NOT PUSH TOO HARD FOR PARTICIPATION, WE WANT TO LEAVE THE DOOR OPEN FOR ANOTHER INTERVIEWER TO TRY. NOTE THE OUTCOME OF THE CONTACT ON THE LOG ATTACHED TO THE QUESTIONNAIRE.

I'll start the interview by asking you a few questions about your birthdate and where you have lived.

1. First of all, what is your birthdate?

______ MONTH ______ DAY ______ YEAR 20/

☐ DON'T KNOW 22/

2. When did you move to your current address? 24/

______ MONTH ______ YEAR 26/

☐ DON'T KNOW 28/

IF AFTER JANUARY 1,1980 RECORD ALL PLACES OF RESIDENCE SINCE JANUARY 1, 1980.

2a. What was your most recent address before that? 30/

ADDRESS			DATE MOVED IN		DATE MOVED OUT	
NO.	STREET	CITY	MO	YR	MO	YR

Next I'd like to ask you something about your medical history.

3. Have you ever been told by a doctor that you had any of the following conditions:

				IF YES: Did you take any medication for this?		IF YES: What was it?	
CONDITION	YES 1	NO 2	DK 7	YES 1	NO 2		
Diabetes	☐	☐	☐	☐	☐	__________	32/
Asthma	☐	☐	☐	☐	☐	__________	36/
Hypertension or high blood pressure	☐	☐	☐	☐	☐	__________	40/
Thyroid	☐	☐	☐	☐	☐	__________	44/

Now some questions about all your pregnancies.

4. How many times have you been pregnant, even if only for a short time?

______ TIMES IF NEVER, TERMINATE INTERVIEW. 48/

5. Did any of these pregnancies result in a miscarriage, stillbirth, or spontaneous abortion, even if it was very early in your pregnancy?

^{1}☐ YES: 5a. How many times have you had a miscarriage, stillbirth, or spontaneous abortion?

_____ TIMES

^{2}☐ NO

6. How many times have you been pregnant since January 1, 1980?

_____ TIMES

6a. Starting with the most recent of these, can you tell me when each of these started and ended?

STARTED	ENDED	STARTED	ENDED

6b. Does this include all your pregnancies since January 1, 1980 including any which started before that date but lasted into 1980?

IGNORE PREGNANCIES WHICH STARTED AFTER DECEMBER 31, 1981 OR ENDED BEFORE JANUARY 1, 1980. RESUME THE INTERVIEW WITH THE MOST RECENT OTHER PREGNANCY.

I'd like to ask you a series of question about the pregnancy that ended

_________________________.

7. When this pregnancy ended were you living at your current address?

^{1}☐ YES

^{2}☐ NO: Did you live in San Jose?

^{1}☐ YES: What was your street address?

____

^{1}☐ IF OUTSIDE STUDY AREA, TERMINATE INTERVIEW.

^{2}☐ IF INSIDE STUDY AREA CONTINUE WITH QUESTION 8.

^{2}☐ NO. TERMINATE INTERVIEW.

8. How far along were you in your pregnancy when you or your doctor decided you were pregnant?

MONTH OF PREGNANCY 66/

[ ] DON'T KNOW

9. Did you have a pregnancy test?

1[ ] YES: 9a. Was this at home, at a doctor's office, or at a hospital or clinic? 68/

1[ ] HOME 69/

2[ ] DOCTOR'S OFFICE

3[ ] HOSPITAL OR CLINIC

4[ ] OTHER (DESCRIBE)

____

9b. Was this done on urine or blood?

1[ ] URINE 70/

2[ ] BLOOD

3[ ] DON'T KNOW

2[ ] NO

7[ ] DON'T KNOW

10. Did this pregnancy end with a live birth, a miscarriage, a spontaneous abortion, a stillbirth or an elective abortion?

1[ ] LIVE BIRTH: SKIP TO QUESTION 14, PAGE 6. 71/

2[ ] MISCARRIAGE OR SPONTANEOUS ABORTION

10a. Did you see a physician for this?

1[ ] YES 2[ ] NO 72/

10b. Do you know what caused the miscarriage or spontaneous abortion?

1☐ YES: EXPLAIN ______________________ 73/

SKIP TO QUESTION 12, NEXT PAGE. 74/

2☐ NO: SKIP TO QUESTION 12, NEXT PAGE.

3☐ STILLBIRTH

10c. Did you see a physician for this?

1☐ YES 2☐ NO 76/

10d. Where did the stillbirth occur?

______________________________ 77/
NAME OF HOSPITAL

10e. Do you know what caused the stillbirth?

1☐ YES: EXPLAIN ______________________ 79/

SKIP TO QUESTION 12, NEXT PAGE. 80/

2☐ NO: SKIP TO QUESTION 12, NEXT PAGE.

4☐ ELECTIVE ABORTION

7☐ DON'T KNOW: INTERVIEWER PROBE REQUIRED.

EXPLAIN: ______________________________ 82/

11. Did a medical person suggest you end the pregnancy early for medical reasons?

1☐ YES: 11a. What was the reason? 84/

______________________________ 85/

____

2☐ NO

87-91/BL

12. Would the baby have had any birth defects or abnormalities?

1[ ] YES: 12a. What did the doctor say it was? 92/

PROBE FOR SPECIFIC CONDITION

____

____

12b. Does any blood relative of the child have this condition?

1[ ] YES: 12c. What relationship is the person to the child? 93/

____________________________ 94/

2[ ] NO

2[ ] NO

7[ ] DON'T KNOW

13. How long were you pregnant?

______ 96/
MONTHS

SKIP TO QUESTION 26.

14. Was the birth a single child or twins?

1[ ] SINGLE BIRTH 98/

2[ ] TWINS: IF TWINS, USE TWIN FORM FOR SECOND BABY.

15. Was the baby a boy or a girl?

1[ ] BOY 99/

2[ ] GIRL

16. What name appears on the baby's birth certificate?

____ 100/

17. When was the baby born?

____ MO ____ DAY ____ YEAR 102/

☐ DON'T KNOW 104/

18. Where was the baby born? 106/

____
NAME OF HOSPITAL OR STREET ADDRESS 108/

☐ DON'T KNOW

19. When was the baby due?

____ MO ____ DAY ____ YEAR 110/

☐ DON'T KNOW 112/

20. How much did the baby weigh? 114/

____ LB ____ OZ 116/

☐ DON'T KNOW: 20a. Do you remember whether the child weighed more or less than 5 1/2 pounds at birth? 122/

1☐ MORE

2☐ LESS

7☐ DON'T KNOW

21. Did the baby cry within five minutes after birth?

1☐ YES 2☐ NO 7☐ DON'T KNOW 123/

22. Was the baby pink within five minutes after birth?

1☐ YES 124/

2☐ NO

7☐ DON'T KNOW

23. Did the baby have any abnormalities or birth defects noticed at the time of birth? (INCLUDE BIRTH MARKS.)

1☐ YES: 23a. What did the doctor say it was? 125/

PROBE FOR SPECIFIC CONDITION.

____

____

23b. Does any blood relative of the child have this condition?

1☐ YES: 23c. What relationship is the person to the child? 126/

_________________________ 127/

2☐ NO

2☐ NO

24. Were any birth defects noticed during the first six months of life?

1☐ YES: 24a. What did the doctor say it was? 129/

____

____

____

____

____

24b. Does any blood relative of the child have this condition?

1☐ YES: 24c. What relationship is the person to the child? 130/

______________________________ 131/

2☐ NO

2☐ NO

25. Is this child alive today?

1☐ YES 133/

2☐ NO: 25a. When did the child die?

_____ MONTH _____ DAY _____ YEAR 134/

25b. What was the cause of death? 136/

______________________________ 138/

______________________________ 140/

25c. Where did the death occur?

IF CALIFORNIA: ______________ COUNTY 145/

IF OUT OF CALIFORNIA: ______________ COUNTY 147/

______________ STATE 149/

26. In the three months before the pregnancy we've been discussing or at any time during this pregnancy were you employed or did you do volunteer work outside your home?

1[ ] YES: 26a. Starting with the most recent, what kind of work did you do? 151/

______________________________ 152/

26b. What were your major duties or activities?

______________________________ 154/

26c. Where did you work?

______________________________ 156/

2[ ] NO

CONTINUE WITH QUESTION 26 BELOW UNTIL PERIOD OF THIS PREGNANCY HAS BEEN COVERED, THEN CONTINUE WITH QUESTION 27.

26d. What kind of work did you do before this?

______________________________ 158/

26e. What were your major duties or activities?

______________________________ 160/

26f. Where did you work?

______________________________ 162/

26g. What kind of work did you do before this?

______________________________ 164/

26h. What were your major duties or activities?

______________________________ 166/

26i. Where did you work?

______________________________ 168/

27. I'm going to read a list of different kinds of substances or materials that some people are exposed to either on a job or in a hobby. For each one, please tell me whether you were regularly exposed to it during this pregnancy or in the three months before.

IF YES: Were you exposed to [NAME OF SUBSTANCE] before pregnancy or during pregnancy?

READ ENTIRE LIST BEFORE ASKING 'IF YES' QUESTIONS.	YES 1	NO 2	DK 7	BEFORE PREGNANCY 1	During what months of pregnancy?	What were you doing?	How often?	
Paint, lacquer or varnish	☐	☐	☐	☐				170/
Organic chemicals or solvents	☐	☐	☐	☐				177/
Asphalt	☐	☐	☐	☐				184/
Gasoline, kerosene, fuel oil, or other petroleum products	☐	☐	☐	☐				191/
Cutting, cooling or lubricating oils	☐	☐	☐	☐				198/
Pesticides or insect sprays	☐	☐	☐	☐				205/
Herbicides or weed killers	☐	☐	☐	☐				212/
Asbestos	☐	☐	☐	☐				219/
Metal dust or fumes	☐	☐	☐	☐				226/
Coal dust	☐	☐	☐	☐				233/
Fibrous glass or glass wool	☐	☐	☐	☐				240/
X-ray or radioactive material	☐	☐	☐	☐				247/
Sand blasting	☐	☐	☐	☐				254/
Other hazardous substances	IF NONE WRITE 'NO'.			☐				261/
								268/
								275/

IN THE FOLLOWING QUESTIONS WE ARE NOT LOOKING FOR OCCUPATIONAL EXPOSURES.

28. In the three months before this pregnancy or at any time during this pregnancy did you have any of the following x-rays:

IF YES: Was this before or during pregnancy?

	YES 1	NO 2	DK 7	BEFORE PREGNANCY 0	During what month of pregnancy?	
Dental?	☐	☐	☐	☐	________	282/
Chest?	☐	☐	☐	☐	________	285/
Pelvic or abdominal?	☐	☐	☐	☐	________	288/
Any other X-ray exposure?	☐	☐	☐	☐	________	291

29. In the three months before the pregnancy or at any time during this pregnancy did you have any of the following:

IF YES: Was this before or during pregnancy?

	YES 1	NO 2	DK 7	BEFORE PREGNANCY 0	During what month of pregnancy?	
Rubella (German measles)?	☐	☐	☐	☐	________	294/
Kidney infection?	☐	☐	☐	☐	________	297/
Anything else with a fever of 101 degrees lasting for at least two days?	☐	☐	☐	☐	________	300/

What was this? ______________________________

30. During this pregnancy did you have any of the following:

	YES *1*	NO *2*	DK *7*	IF YES: During what month of pregnancy?	
Pre-eclampsia?	☐	☐	☐	________	303/
Eclampsia?	☐	☐	☐	________	306/
Toxemia of pregnancy?	☐	☐	☐	________	309/
Hypertension?	☐	☐	☐	________	312/
Seizures?	☐	☐	☐	________	315/

31. In the three months before the pregnancy we've been discussing, or at any time during this pregnancy did you have any other illnesses, or contagious diseases for which you saw a doctor?

1☐ YES: 31a. What was this? 318/

______________________________ 319/

____

31b. When did this start?

______ MONTH ______ YEAR 321/

31c. When did this condition end?

______ MONTH ______ YEAR 325/

2☐ NO

32. During this pregnancy, did you take any of the following pills or medication?

32a. Anti-nausea pills? *1*☐ YES *2*☐ NO *7*☐ DON'T KNOW 329/

IF YES: What was this? (BRAND NAME)	What month of pregnancy did you start taking this?	What month of pregnancy did you stop taking this?	How many times a week?	
______________	__________	__________	______	330/
______________	__________	__________	______	336/
______________	__________	__________	______	342/

32b. Sleeping pills? 1[ ] YES 2[ ] NO 7[ ] DON'T KNOW 348/

IF YES:	What was this? (BRAND NAME)	What month of pregnancy did you start taking this?	What month of pregnancy did you stop taking this?	How many times a week?	
					349/
					355/
					361/

32c. Diet pills 1[ ] YES 2[ ] NO 7[ ] DON'T KNOW 367/

IF YES:	What was this? (BRAND)	What month of pregnancy did you start taking this?	What month of pregnancy did you stop taking this?	How many times a week?	
					368/
					374/
					380/

32d. Tranquilizers 1[ ] YES 2[ ] NO 7[ ] DON'T KNOW 386/

IF YES:	What was this? (BRAND NAME)	What month of pregnancy did you start taking this?	What month of pregnancy did you stop taking this?	How many times a week?	
					387/
					393/
					399/

32e. Estrogens? 1[ ] YES 2[ ] NO 7[ ] DON'T KNOW 405/

IF YES:	What was this? (BRAND NAME)	What month of pregnancy did you start taking this?	What month of pregnancy did you stop taking this?	How many times a week?	
					406/

410-421/BL

32f. Dilantin? 1[ ] YES 2[ ] NO 7[ ] DON'T KNOW 422/

IF YES: What was this? (BRAND NAME)	What month of pregnancy did you start taking this?	What month of pregnancy did you stop taking this?	How many times a week?	
				423/

32g. Phenobarbital? 1[ ] YES 2[ ] NO 7[ ] DON'T KNOW 429/

IF YES: What was this? (BRAND NAME)	What month of pregnancy did you start taking this?	What month of pregnancy did you stop taking this?	How many times a week?	
				430/

32h. Any other medication prescribed by your doctor? 1[ ] YES 2[ ] NO 7[ ] DON'T KNOW 436/

IF YES: What was this?	What month of pregnancy did you start taking this?	What month of pregnancy did you stop taking this?	How many times a week?	
				437/
				443/
				449/

32i. Any other drugs not prescribed by your doctor, including recreational drugs, such as diet pills, pain relievers, vitamin supplements, marijuana, cocaine, or LSD?

1[ ] YES 2[ ] NO 7[ ] DON'T KNOW 455/

IF YES: WHAT WAS THIS?	What month of pregnancy did you start taking this?	What month of pregnancy did you stop taking this?	How many times a week?	
				456/
				462/
				468/

33. Did you smoke cigarettes during this pregnancy?

1[ ] YES: 33a. How many packs a day did you smoke: 474/

1[ ] Half a pack a day or less

2[ ] About a pack a day

3[ ] About a pack and a half a day

4[ ] About two packs a day

5[ ] More than two packs a day

7[ ] DON'T KNOW

475/

33b. During what months of pregnancy did you smoke?

476/

____
MONTHS OF PREGNANCY

2[ ] NO

34. Did you drink any type of alcoholic beverages during this pregnancy--any beer, wine, or hard liquor?

1[ ] YES: 34a. About how often did you drink alcoholic beverages during this pregnancy? 478/

1[ ] Once a month or less

2[ ] Several times a month

3[ ] About once a week

4[ ] Several times a week

5[ ] About every day?

6[ ] DON'T KNOW

479/

34b. On days when you did drink alcoholic beverages, about how much did you drink:

1[ ] One drink a day

2[ ] 2-3 drinks a day

3[ ] 4 or more drinks a day?

7[ ] DON'T KNOW

480/

34c. What months during pregnancy did you drink?

481/

____
MONTHS OF PREGNANCY

2[ ] NO

7[ ] DON'T KNOW

Now I'd like to ask about foods you may have eaten or nonalcoholic beverages you may have had during this pregnancy.

35. Of the fruits and vegetables you ate during that pregnancy, what proportion of them came from your garden or from a neighbor's garden?

______ PERCENT OR ______ FRACTION 483/

IF LESS THAN 100 PERCENT CAME FROM OWN OR NEIGHBOR'S GARDEN:

36. Where did you usually buy your fruit and vegetables?

______________________ NAME OF STORE 485/

37. During the pregnancy did you drink coffee regularly?

1[ ] YES: 37a. How many cups a day did you usually drink? 487/

______ CUPS 488/

37b. During what months of your pregnancy did you drink coffee?

______________ MONTHS OF PREGNANCY 490/

37c. Was this regular coffee or caffeine-free coffee?

1[ ] REGULAR COFFEE 492/

2[ ] CAFFEINE-FREE COFFEE

2[ ] NO

38. During the pregnancy did you drink hot tea or iced tea regularly?

1[ ] YES: 38a. How many cups or glasses a day did you usually drink? 493/

______ CUPS OR GLASSES 494/

38b. When during your pregnancy did you drink tea?

______________ MONTHS OF PREGNANCY 496/

2[ ] NO

39. During the pregancy did you drink cola drinks regularly?

1[ ] YES: 39a. How many glasses a day did you usually drink? 498/

499/

______ GLASSES

39b. When during your pregnancy did you drink cola drinks?

______ MONTHS OF PREGNANCY 501/

2[ ] NO

I'm going to ask you some questions now about the water you drank during this pregnancy or for the three months before the pregnancy.

40. Did you use bottled water at all at home during this pregnancy or for the three months before the pregnancy?

1[ ] YES 503/

40a. What brand did you use?

______________________________ 504/

2[ ] NO: SKIP TO QUESTION 42.

41. Did you usually use bottled water at home?

1[ ] YES 505/

41a. What brand did you use?

______________________________ 506/

SKIP TO QUESTION 44.

2[ ] NO

42. How many glasses or cups of cold tap water or beverages made of unheated water did you drink each day, on the average, at home? This should include any beverages made of unheated water such as orange juice, iced tea, or other beverages made from concentrate.

507/

______ GLASSES OR CUPS

43. How many glasses or cups of beverages made from heated tap water did you drink each day, on the average, at home? This should include any beverages that require heating or hot water even though they may be cool when you drink them, for example, iced tea that is brewed with hot water, or iced coffee?

________ GLASSES OR CUPS 509/

Now I'm going ask you some similar questions about the water you drank at work during this pregnancy or in the three months before the pregnancy.

44. Did you use bottled water at all at work during this pregnancy or for the three months before the pregnancy?

1[ ] YES 511/

44a. What brand did you use?

________________________ 512/

2[ ] NO: SKIP TO QUESTION 47.

45. Did you usually use bottled water at work during this pregnancy or for three months preceding this pregnancy?

1[ ] YES 513/

45a. What brand did you use?

________________________ 514/

SKIP TO QUESTION 49.

2[ ] NO

47. How many glasses or cups of cold tap water or beverages made of unheated water did you drink at work each day, on the average, during this pregnancy or in the three months before the pregnancy? This should include any beverages made of unheated water such as orange juice, iced tea, or other beverages made from concentrate.

________ GLASSES OR CUPS 515/

48. How many glasses or cups of beverages made from heated tap water did you drink at work each day, on the average, during this pregnancy or in the three months before the pregnancy? This should include any beverages that require heating or hot water even though they may be cool when you drink them, for example, iced tea that is brewed with hot water, or iced coffee?

________ GLASSES OR CUPS 517/

49. Did you use a community swimming pool during this pregnancy or in the three months before?

1☐ YES: 49a. Where is this located? 519/

________________________________ 520/

49b. On the average, how many hours a week were you in the water?

HOURS 521/

2☐ NO

50. Did you use a private swimming pool during this pregnancy or in the three month before?

1☐ YES: 50a. Where is this located? 523/

1☐ OWN YARD

2☐ ELSEWHERE (DESCRIBE) 524/

____

50b. On the average, how many hours a week were you in the water?

HOURS 526/

2☐ NO

51. During the three months preceding this pregnancy were you or the father using any form of birth control--anything to delay or prevent you from getting pregnant?

1☐ YES: 51a. What method was this? 528/

529/

1☐ PILL

2☐ IUD

3☐ OTHER: What was this?

____

7☐ DON'T REMEMBER

2☐ NO

52. Did you stop using a birth control method in order to become pregnant?

1☐ YES: 52a. About how long was it between the time you stopped using this birth control method and the time you became pregnant? 530/

____ YEARS ____ MONTHS 531/

2☐ NO

Now I'd like to ask you a few questions about the father of the pregnancy we've been discussing.

53. What kind of work did the father usually do during this pregnancy?

____ 535/

53a. What were his major duties or activities?

___________________________ 537/

53b. Where did he work?

___________________________ 539/

54. Did the father serve in the armed forces in Vietnam?

1☐ YES 541/

2☐ NO

55. In what country was the father born?

__________________________________ 542/

56. In what religion was he raised?

1☐ PROTESTANT

2☐ CATHOLIC

3☐ JEWISH

4☐ LATTER DAY SAINTS (MORMONS)

5☐ OTHER: DESCRIBE ________________

6☐ NONE

7☐ DON'T KNOW

544/

57. Which of the following best describes his race or ethnic group:

1[ ] Hispanic
2[ ] Black
3[ ] White
4[ ] American Indian
5[ ] Asian
6[ ] Or some other group?
(What is this?) ____________________
7[ ] DON'T KNOW

545/

58. What is the highest grade in school that he completed?

1[ ] 0-8 546/
2[ ] 9-11
3[ ] 12 (HIGH SCHOOL GRADUATE)
4[ ] 13-15 (SOME COLLEGE OR TECHNICAL SCHOOL)
5[ ] 16 or more (COLLEGE GRADUATE)
7[ ] DON'T KNOW

59. Are you and the father of this pregnancy related by blood?

1[ ] YES: 59a. In what way? 547/
____ 548/
2[ ] NO

I'D LIKE TO CONCLUDE WITH A FEW MORE QUESTIONS ABOUT YOURSELF.

60. Have you had any babies with birth defects that have not been included in the interview?

1[ ] YES: Which birth defects were these? 549/
____
2[ ] NO

61. Have you had any miscarriages, spontaneous abortions, stillbirths, or elective abortions that have not been included in the interview, but that would have resulted in a baby with a birth defect or abnormality?

1[ ] YES: What were these? ______________________ 550/

2[ ] NO

62. What is your current marital status? Are you:

1[ ] Married

2[ ] Separated or divorced

3[ ] Widowed

4[ ] Never married 551/

63. In what country were you born?

______________________ 552/

64. In what religion were you raised?

1[ ] PROTESTANT

2[ ] CATHOLIC

3[ ] JEWISH

4[ ] LATTER DAY SAINTS (MORMONS)

5[ ] OTHER: DESCRIBE ______________________

6[ ] NONE

7[ ] DON'T KNOW 554/

65. Which of the following best describes your race or ethnic group:

1[ ] Hispanic

2[ ] Black

3[ ] White

4[ ] American Indian

5[ ] Asian

6[ ] Or some other group? (What is this?) ______________________

7[ ] DON'T KNOW 555/

66. What is the highest grade in school that you have completed?

1[ ] 0-8 556/

2[ ] 9-11

3[ ] 12 (HIGH SCHOOL GRADUATE)

4[ ] 13-15 (SOME COLLEGE OR TECHNICAL SCHOOL)

5[ ] 16 or more (COLLEGE GRADUATE)

7[ ] DON'T KNOW

If we need to get in touch with you again, can you give me the name and address of a relative, friend, or organization who would be apt to know how we can reach you if you move away?

____

____ 557/

Do you have any questions you'd like to ask me before we finish the interview?

ANSWER QUESTIONS OR REFER TO A SUPERVISOR.

Thank you very much for helping us in this study.

TIME INTERVIEW FINISHED ____________

COMMENTS ____________________________________

____

____

____

____

DHS/ESS/MD/05/23/83

APPENDIX B

TOXICOLOGICAL REVIEW

1,1,1-Trichloroethane
Summary of Data on Teratology and Reproductive Effects Studies

Species	Route	Exposure	Results
1. Rat (Sprague-Dawley)	Inhalation	875 ppm 7 hr/day d 6-15 of gestation	No effects on body weight, food consumption, relative liver weight, average number of implantation sites per litter, litter size, fetal resorption, fetal sex ratios, fetal body body measurements, gross anomalies, soft tissue changes, skeletal anomalies, organs, tissues, cells. Significant increase in absolute liver weight compared to controls.
Mouse (Swiss Webster)	Inhalation	875 ppm 7 hr/day d 6-15 of gestation	Same findings as in rats but no effect on absolute liver weight
2. Mouse (ICR Swiss)	Oral Drinking water	0, 100, 300, or 1,000 mg/kg/day Two-generation	No effects on fluid consumption, body weight, fertility, gestation, litter size, viability, lactation. Sporadic maternal mortality. No dominant lethal effect nor teratogenic effect.
3. Rat (Long-Evans)	Inhalation	Exposure to 2100 ppm: a) Before and after mating (++ group), 6 hr/day, 5 days/week for 2 weeks and then 7 days/week through day 20 of pregnancy b) Before mating (+-group), 6 hr/day, 7 days/week for 2 weeks c) during pregnancy (-+ group), 6 hr/day, 7 days/week through day 20 d) filtered air before mating and during pregnancy (-- group) Half of the animals evaluated for teratogenicity (sacrificed on d 21) and half for neurotoxicity (parturition on d 22-23 of pregnancy)	Teratology evaluation: Significantly increased weight gain during pregnancy in (-+) group. Significant depression in total fetal body weight and male fetal body weight in (-+) and (++) groups. Significant elevation in the total number of variations (delayed ossification of sternum, rudimentary ribs) and minor skeletal anomalies (reduced clavicle size, missing or unossified 13th rib, wavy ribs, missing or unossified 26th and 27th vertebrae, incomplete braincase closure) in (++) group. Significant elevation in the total number of minor visceral anomalies (hemorrhagic pericardium, small kidney, hydronephrotic kidney, enlarged renal medulla) in (++) group.

			Neurotoxicity evaluation: No effect on post-natal body weight or survival (1 to 12 mo of age). No significant differences observed in neurobehavioral tests of open-field activity (21 d of age), running wheel activity (40-110 d of age), and an amphetamine challenge test (110-120 d of age). Gross lesions observed at 12-mo autopsy were comparable in all groups
4. Chick embryo	Injection into air sac	5,25,50,100 umol/egg at 3 or 6 days of age	Dose-related decrease in survival. Not dose-related increase in % of malformed survivors
5. Mouse	Intratesticular injection	100,1000 mg/kg	Dose-related increase in tritiated thymidine pool size and decrease in testicular DNA synthesis

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1,1-Dichloroethylene
(Vinylidene Chloride)
Summary Data on Teratology and Reproductive Effect Studies

Species	Route	Exposure	Results
1a. Rat (Sample sizes of 44,30,30 in increasing (order of exposure)	Inhalation	0,20,80,160 ppm, 7 hr/day, at d 6-15 of gestation	At 80 and 160 ppm, maternal weight gain decreased during exposure period, and increased during post-exposure period; similar trends in food consumption. Increase in liver to body weight ratio at 160 ppm. No effect on outcome of pregnancy as indicated by number of implants, live fetuses, resorption rates, fetal sex ratios, fetal weight. No increase in major malformations. Wavy ribs and delayed ossification noted as feto-and embryotoxic manifestations of maternal toxicity at 80 and 160 ppm.
1b. Rat (N=26 for control and 24 for treated)	Oral (Drinking Water)	0,200 ppm (Daily doses of 40 mg/kg equivalent to a single 7-hr inhalation exposure to 120 ppm)	No effect on outcome of pregnancy. Significant increase in crown-rump length in fetuses.
1c. Rabbit (N =16,23, 18, in increasing order of exposure)	Inhalation	0,80, 160 ppm, 7 hr/day, at d 6-18 of gestation	At 160 ppm, body weight gain decreased during exposure and increased after termination of exposure. Increased liver to body weight ratio at 80 ppm. Increased resorption rate at 160 ppm correlated with maternal weight loss, suggestive of effect secondary to maternal toxicity. No major malformations.

2.	Rats (Sprague-Dawley) N=10 males and 30 females in control group	Oral (Drinking Water)	0,50,100,200 ppm 3-generation	No adverse effect on reproduction or neonatal development. Decreased neonatal survival in F3A litters, but contradictory results in F3b and F3c litters.
3a.	Rat (N=18 to 20 in treatment group. 60 in control group.	Inhalation	0,15,57,300,449 ppm 23 hr/day, at d 6-16 of gestation	Deaths (>25%) at 300 to 449 ppm no effect on weight gain and food consumption in all treated groups. Resorptions at 37 and 449 ppm. No gross external abnormalities. Fetotoxicity (soft tissue anomalies and skeletal ossification problems) in all groups but could not be evaluated for teratogenicity because maternal toxicity seen.
3bi.	Mouse	Inhalation	0,15,30,57,144, 300ppm 23 hr/day at d 6-16 ot gestation	Deaths (100%) at 144 and 300 ppm. Reduction of weight gain and food consumption at 30 ppm and above Resorptions at 30 and 57 ppm. No gross external abnormalities. Fetotoxicity (skeletal ossification problems) in all groups but could not be evaluated for teratogenicity because maternal toxicity seen.
3bii.	Mouse (N =10-24)	Inhalation	41-112ppm (Varying combination of exposure levels and exposure periods)	Shortened exposure period lessened resorption but treatment related weight loss still evident. Soft tissue and skeletal anomalities seen but not statistically significant and occurred only when maternal welfare had been adversely affected by DCE exposure. Behavorial studies showed no major adverse effects.

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